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13. ABSTRACT *(Maximum 200*

Southern Research Institute tested the feasibility of making biodegradable, time-release, pharmaceutical microspheres in space. Based on experiments conducted on Space Shuttle Discovery (Mission STS-53: December, 1992), we modified, built, safety tested, and flew hardware we call the Microencapsulation in Space (MIS-B) experiment.

The MIS-B experiment flew on Space Shuttle Discovery -- Mission STS-70. Before launch, NASA technicians removed two storage lockers and in their place mounted the MIS-B hardware. Launch date was July 13, 1995. We retrieved the MIS-B hardware on July 20, 1995.

The microspheres were characterized visually, by scanning electron microscopy, atomic spectroscopy, and differential scanning calorimetry. The space-made, ampicillin-loaded microspheres were more spherical, had smoother surfaces, and had better internal organization that earth-made microspheres of the same composition. From our experience, these improved properties should improve the release properties of microencapsulated drugs and eliminate unwanted residual process aids. Furthermore, it is likely that microencapsulation in space will let us encapsulate drugs that can not be microencapsulated on earth. In a more general sense, we believe that a wide variety of materials -- speciality chemicals as well as pharmaceuticals, liquids and solids -- can be microencapsulated in space and potentially afford microsphere products with unique and superb performance properties.

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Thomas R. Lee 27 September 1996

PI Signature Date

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MICROENCAPSULATION OF DRUGS IN THE MICROGRAVITY ENVIRONMENT OF THE UNITED STATES SPACE SHUTTLE - FOLLOW ON EXPERIMENTS

I. INTRODUCTION

The United States Army Institute of Dental Research (USAIDR) contracted Southern Research Institute (Southern Research) to design and construct an improved experiment to test the feasibility of making time-release, antibiotic microspheres in space. The experiment was called "Microcapsules in Space" or "MIS". The experiment hardware was called "MIS-B". An exploded diagram of the MIS-B is shown on the next page.

MIS-B hardware is an improved version of MIS-A hardware. MIS-A was designed and constructed during Southern Research's first MIS contract (DAMD17-89-C-9035). MIS-A flew aboard the U.S. Space Shuttle Discovery, Mission STS-53, on December 2, 1992. What we learned from MIS-A was used to improve the configuration and operation of MIS-B. MIS-B flew aboard the U.S. Space Shuttle Discovery, Mission STS-70, on July 13, 1995.

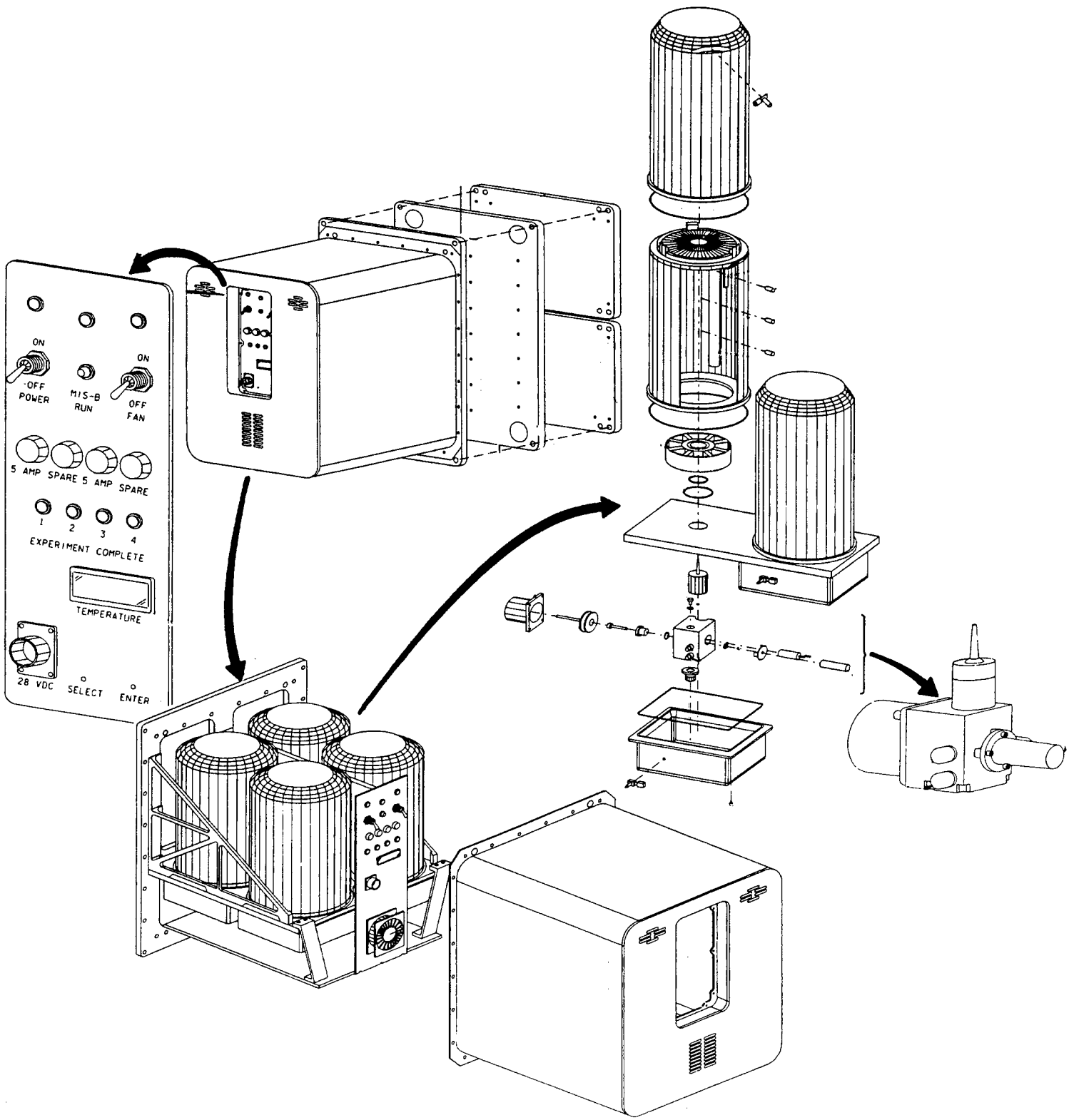
The MIS-B experiment was designed to fit in the middeck of the United States Space Shuttle. It occupies the space of two standard space shuttle middeck lockers. The design goal of MIS-B was to obtain a larger yield of microspheres than that obtained on MIS-A.

The global objective of the MIS experiments was to demonstrate the feasibility of producing pharmaceutical microspheres in a microgravity environment. To meet this objective, a drug, ampicillin anhydrate, was microencapsulated in space. Because ampicillin anhydrate microspheres can be made on earth, it's possible to compare the characteristics of earth-made with space-made microspheres. During the MIS-A project, we showed that the manufacturing microspheres in the microgravitation environment of space can improve the quality of the microspheres.

Knowledge gained by this research could indicate whether pharmaceuticals which can not be microencapsulated on earth due to solvent incompatibilities or diffusional dilution can be easily microencapsulated in space. Microencapsulation would enable these drugs to be administered in a controlled-release fashion which could greatly increase their therapeutic value. Research conducted at the U.S. Army Institute for Dental Research (USAIDR) has indicated that antibiotics microencapsulated in poly(DL-lactide-co-glycolide) microspheres control wound infections *in vivo* following a single application of the microspheres directly to the wound. Consequently, controlled-release antibiotic microspheres could have great utility in treating wounds caused during battle.

The space-made microspheres were smoother and denser inside than the microspheres made on earth. The crystallinity of the space-made microspheres and earth-made microspheres were similar.

MICROENCAPSULATION IN SPACE HARDWARE



Below is a list of the specific tasks completed on this contract.

Task 1: The literature search started under the initial contract was continued. With the incorporation of new systems into the experimental hardware, more references describing the current knowledge of these systems were required.

Status: Completed.

Task 2: Improvement MIS-B hardware over MIS-A hardware.

Status: Completed. Improvements to the MIS-B hardware include:

- ✦ Integrating the plumbing system into a compact unit containing all the components
- ✦ Designing each hardening chamber to possess individual primary and secondary containment systems
- ✦ Constructing the hardening chamber from aluminum
- ✦ Designing a control circuit expressly for MIS-B which replaces the programmable logic controller used in MIS-A
- ✦ Redesigning the outer cover and control panel
- ✦ Incorporating active cooling into MIS-B
- ✦ Incorporating a fan and duct system in each hardening chamber to improve air circulation and distribution of microdroplets
- ✦ Using helium to provide a method of leak detection superior to that use on MIS-A; nitrogen would still be used as a backfilling gas to inert the hardware
- ✦ Coating the inside surface of the hardening chambers with a fluorosilicone compound to prevent the polymer/drug suspension microdroplets from sticking to the hardening chambers
- ✦ Removing the video recording system and fiber optic lighting system

- ✦ Removing the electrostatic containment system
- ✦ Switching to ethyl acetate as the polymer solvent (methylene chloride was used in MIS-A). Changing the adsorbent from Type A molecular sieves to silica gel
- ✦ Reducing the x-axis dimension by 0.875 in. to bring MIS-B in compliance for payload envelope
- ✦ Reducing the weight to bring MIS-B in compliance for payload weight
- ✦ Increasing the number of experiments in MIS-B from two to four
- ✦ Increasing the concentration of poly(DL-lactide-co-glycolide) in the polymer/drug suspension from 5.0 wt % to 7.5 wt %

Task 3: Characterization of the polymer used in the space-made microspheres.

Status: Completed. We found the space-made microspheres were smoother and more dense inside than microspheres made on earth.

Task 4: Selection of drug to be microencapsulated in microgravity.

Status: Completed. Ampicillin anhydrate was used in the experiments.

Task 5: Equipment review and fabrication.

Status: Completed. Equipment fabrication was completed in December, 1995.

Task 6: Safety reviews and flight certification.

Status: Completed. Flight certification was granted by NASA after successful completion of the preflight ground operations on July 7, 1995, for the second launch of STS-70. In addition, flight certification was granted by NASA after successful completion of the preflight ground operation for the first launch attempt. The first launch attempt for STS-70 was scrubbed three days before the scheduled launch.

Task 7: Flights and flight debriefings.

Status: Completed. MIS-B flew on board STS-70 which had lift-off on July 13, 1995. Landing occurred on July 20, 1995. The MIS-B hardware functioned as expected during the mission. Subsequent analysis of the hardware after the mission indicated some problems which limited the yield of microspheres.

Task 8: Analysis of space-made microspheres.

Status: Completed. The microspheres were characterized with respect visually, by scanning electron microscopy, atomic spectroscopy, and differential scanning calorimetry.

During the first half of the research program, we changed the design of the MIS-B hardware and software to incorporate the results obtained from MIS-A. These design changes are listed above in Task 2. Some of the more important changes to the design were performed to bring MIS-B in compliance with NASA specifications with regard to payload envelop and weight. In addition, the safety review process to which the MIS-A hardware was subjected gave the MIS-B design team important insights as to how to redesign MIS-B to accommodate NASA safety requirements. A description of these modifications are summarized later in this report.

We participated in numerous meetings involving the MIS-B integration team from the U.S. Air Force, Aerospace Corporation, Dynetics, Inc., and Muniz Engineering, Inc., and the appropriate NASA personnel. These meetings were part of the process of redesigning MIS-B with as many inputs from NASA personnel and other members of the integration team. These meetings also involved introducing MIS-B into the NASA payload integration and manifestation procedure.

We performed additional experiments on the operation of the MIS-B hardware to confirm that the polymer concentration can be increased while maintaining the same core loading of drug as was used in MIS-A. By increasing the polymer concentration, a higher yield of microspheres is potentially possible and less solvent adsorbent is needed. These experiments indicated that the polymer concentration can be increased to 7.5 wt % when ethyl acetate is used as the solvent. In MIS-A, methylene chloride was used as the polymer solvent. Because of the low boiling point of methylene chloride and the heat generated by the ultrasonic nozzle, a lower concentration of polymer and a faster pump-rate through the ultrasonic nozzle had to be used to prevent precipitation of the polymer on the ultrasonic nozzle tip. By using ethyl acetate as the polymer solvent, a slower spray rate and a higher polymer concentration were possible due to the higher boiling point of ethyl acetate compared to methylene chloride.

On May 12, 1994, we briefed the Space Test Program (STP) DoD Space Experiment Review Board. Along with discussing the military relevancy and need for space flight issues at this briefing,

we also presented the latest engineering drawings. However, eight of the programs ranked above MIS-B do not have full funding.

During the second half of the research program, we concentrated on the activities required to manifest MIS-B aboard the space shuttle. One of these activities was to modify the leak-check procedure to enable faster seal integrity testing of the MIS-B hardware required to be performed during the prelaunch ground operations. For MIS-A, we used a pressure-decay method to test seal integrity. Although this method is acceptable as a seal-integrity test, it requires an extended period of time to provide valid results. Therefore, we investigated using helium-leak testing as a method to test seal integrity. Helium-leak testing is inherently more accurate and can be performed faster than pressure-decay testing.

Helium-leak testing involves pressurizing the containment systems of MIS-B with helium after they have been assembled into their preflight configuration. Then, a leak detector is passed along the containment vessel seams. The detector uses differences in thermal conductivity to detect leaks. After preliminary experiments and collaborating with the MIS-B integration team, we decided that helium-leak testing could be effectively used to test MIS-B seal integrity. In addition, we discussed using helium as the backfilling gas to inert the containment systems of the MIS-B hardware as required by NASA safety regulations. But, we decided that nitrogen backfilling would be a better choice due to the increased mobility of helium molecules as opposed to nitrogen molecules. The increased mobility of helium may allow for a faster loss through the seals of the containment systems than nitrogen.

We instituted the safety-review procedure necessary to achieve flight certification by NASA with the Phase 0/1 Safety Review held October 27, 1994. During this safety review, the MIS-B integration team presented the hardware and the safety validation documentation to the NASA safety review personnel for review and comment. After reviewing the documentation and hardware, NASA safety personnel decided that additional safety reviews would not be needed due to the fact that MIS-B is a follow-on to already flight-certified hardware (MIS-A). Usually, two more safety reviews (Phase 2 and Phase 3) are required for the approval of flight hardware.

With the successful Phase 0/1 Safety Review, we concentrated on completing the construction of the MIS-B hardware during the last quarter of 1995. Construction was completed in December, 1995. Immediately following the completion of MIS-B hardware, we performed preliminary structural, seal, and functionality tests. These tests were performed during December, 1995 and January, 1996. Positive test results were required by U.S. Air Force members of the MIS-B integration team to verify that fully functional equipment was available for the required NASA safety testing and for insertion into the NASA manifestation queue for a future space shuttle flight opportunity. This testing revealed that the MIS-B hardware was ready for the safety testing and for preliminary manifestation aboard STS-70.

Four safety tests were required by NASA for all flight hardware: an electromagnetic interference (EMI) test, an off-gassing test, an acoustic test, and a rapid-depressurization test. The testing began in January, 1995.

The first safety test performed on the MIS-B hardware was the EMI test. The EMI test was conducted on January 18, 1995. The EMI test consists of nine separate tests. During these tests, the MIS-B hardware passed six of nine tests. Although we could have obtained a variance for two of the tests that failed, NASA usually does not grant a variance for hardware which fails the other test (the transient power-on tests). We encountered similar problems with the MIS-A hardware which was traced to the simultaneous power-up of the individual components of the electronic system. Therefore, we knew what modifications to the control program and electrical circuits could be realized to correct the power-up sequence problems identified during EMI testing. With these modifications to the MIS-B hardware, we retested on March 16, 1995. The hardware passed the transient power-on test and had minor exceedances on two of other repeated tests (conducted EMI). Variances were granted by NASA for these exceedances.

Acoustic test of the MIS-B hardware was held on January 19, 1995. The hardware had minor exceedances at three frequencies but NASA granted a variance for these exceedances. However, NASA could not verify the results immediately and the issue was listed on the verification tracking log (VTL) until NASA safety personnel could close the item.

The rapid depressurization test was held on February 8, 1995. The preliminary results of this test indicated that the MIS-B hardware could withstand an emergency bail-out condition without a structural failure. Subsequent analysis of the weld seams indicated that no stress fractures occurred as a result of the rapid depressurization.

Off-gassing test of the MIS-B hardware was held on February 11, 1995. The off-gassing test involves heating the hardware in a controlled environment and sampling the gasses that evolve. The MIS-B hardware passed this test. However, NASA could not verify the results immediately and the issue was listed on the VTL until NASA safety personnel could close the item.

During the safety testing of MIS-B hardware, we drafted preflight and postflight ground operations protocols in collaboration with MIS-B integration team. These protocols are required and reviewed by NASA safety personnel to insure that an effective procedure is established for assembling the hardware for launch and for disassembling the hardware after landing. The protocols are also necessary to close out items on the VTL. Successful closure of all open items identified in the VTL is required before the hardware in stowed aboard the space shuttle. In addition to drafting these protocols, the integration team also performed the procedures to identify flaws, to reorganize steps in a more logical progression, and to practice the procedure for the actual flight.

The verification tracking log was established for the MIS-B hardware. MIS-B was granted tentative manifestation aboard STS-70 pending final safety certification by NASA to be granted by successfully closing all VTL items. The VTL items were:

- Analysis of offgassing test data by NASA
- Bond and isolation resistance measurement
- Battery circuit review by NASA
- Hardware fit check
- Analysis of acoustic test data by NASA
- Successful performance of prelaunch ground operations

One open item identified in the VTL was determining the bond and isolation resistance of the MIS-B hardware. The bond resistance test insures that any static charge that accumulates on any surface in the hardware can be dissipated through the hardware mounting system. Isolation resistance test insures that the electrical system of the hardware is grounded only through the ground wire on the power cable. These tests were performed April 7 and May 18, 1995. The MIS-B hardware passed these tests.

On May 4, 1995, we briefed the Space Test Program (STP) DoD Space Experiment Review Board. Along with discussing the military relevancy and need for space flight issues at this briefing, we presented the final engineering drawings.

To insure that MIS-B could be installed in the space shuttle, the hardware was installed in its anticipated mounting location on the forward wire trays of Discovery on April 15, 1995. The fit check showed no mounting abnormalities.

The first launch attempt of STS-70 was on June 8, 1995. The preflight ground operations were successfully performed and all open items on the VTL were closed. However, the launch scrubbed three days prior to scheduled launch date due to problems associated with the shuttle's external fuel tank. Woodpeckers were stripping the insulation from the external tank.

The second launch attempt of STS-70 was on July 13, 1995. Again, the preflight ground operations were successfully performed with closure of the VTL and the launch was successful. On orbit, MIS-B hardware operated on Day 5 of mission and functioned as expected. The MIS-B hardware was recovered on July 20, 1995, and postflight ground operations were performed. We recovered a small amount of space-made microspheres during the postflight ground operations. The amount recovered was smaller than anticipated. We analyzed the hardware and made recommendations concerning its operation and configuration for improving the hardware to increase microsphere yields. Subsequent analysis of the space-made microspheres by Southern Research Institute indicated that the microspheres were significantly different from earth-made microspheres of similar composition. More detail concerning hardware descriptions, results, and conclusions are given in the following sections of this report.

II. BACKGROUND

Microencapsulated drugs (antibiotics) capable of providing precise and predictable sustained drug release rates have been of interest to the Department of Defense. Through the microencapsulation of these pharmaceuticals, more effective and efficient treatment of a variety of casualty situations can be achieved.

Research and development programs pertaining to microencapsulated antibiotics have been conducted at U.S. Army Institute for Dental Research (USAIDR) in collaboration with Southern Research. Antibiotics microencapsulated within poly(DL-lactide-co-glycolide) microspheres have been shown to control wound infections *in vivo* following a single application of the antibiotic microspheres directly to the wound. Consequently, controlled-release antibiotic microspheres should have great utility in treating wounds.

Controlled drug delivery offers profound advantages over conventional dosing. It assures patient compliance and simplifies the dosing regimen by requiring only a single dose for long-term therapy. These characteristics can be seen to be of considerable value in situations where mass casualty may occur. Other advantages of controlled drug delivery include more effective utilization of drugs with short half-lives, reduction of toxic side effects by maintaining the drug concentration within therapeutic values, and drug conservation through a more effective dosing regimen. Microencapsulation can also improve the stability of some drugs allowing for longer shelf-life. Lastly, microencapsulation technology provides a way of delivering new proteins and peptides produced from the emerging biotechnology industry. Presently these types of drugs, can not be delivered in a controlled-release fashion by conventional methods (oral administration).

Certain drugs, however, can not be microencapsulated satisfactorily on earth using current microencapsulation technology. To manufacture microspheres on earth, for example, emulsion-based or spray-drying technologies are often used. Although these processes have been used to microencapsulate drugs, both of these technologies have processing requirements which limit their usefulness. More specifically, emulsion-based processes require an organic solvent that dissolves the polymeric wall material. This organic solvent must be immiscible in water to form an oil-in-water emulsion. This organic solvent must also be nontoxic and compatible with the drug. Once a suitable organic solvent is found, emulsion-based microencapsulation may still be difficult to perform because the drug may leach into the water phase (processing medium) of the emulsion before the microspheres are formed.

Spray-drying technology uses air as the processing medium. As a result, drug is not lost to the processing medium (air) during the formation of the microsphere. However, there is only a limited amount of time available to form and dry the microspheres before they collide with each other or the process equipment. As a result, the solvent must be quickly removed from the forming microspheres. This process often results in poor-quality microspheres because the quick removal of

solvent causes the formation of irregular-shaped microspheres with poor surfaces and numerous interior voids.

Microsphere manufacturing in microgravity will eliminate the need for a liquid process medium (water) as is necessary in emulsion-based microencapsulation. Consequently, more solvents would be available to dissolve the wall polymer because the requirement of immiscibility in water would be eliminated. In addition, drug loss to the processing medium (air) is eliminated as with spray-drying. However, by being able to slowly remove the solvent from the forming microspheres in space, the microspheres should be highly spherical with high-quality surfaces -- a result impossible to achieve with earth-based spray-drying.

III. PURPOSE

The goal of this contract was to design and construct a device that could make pharmaceutical microspheres in space, more specifically, time-release, antibiotic microspheres. The experiment hardware occupied two middeck lockers aboard the United State Space Shuttle. Four experiments were incorporated into the MIS-B hardware. Once in the microgravity environment of space, two experiments tested whether pharmaceutical microspheres could be made by using an ultrasonic spray nozzle to spray a polymer/drug/solvent mixture into a cylinder with subsequent solvent removal. Solvent removal was accomplished through the use of an absorbent. The other two experiments were similar to the first two except that no drug was incorporated into the polymer solution. These experiments served as controls to the experiments using drug.

The design of MIS-B depended heavily on the design of MIS-A, on the experience obtained by the MIS-A integration team during the NASA safety review process for MIS-A, and on the results obtained from the successful operation of MIS-A on-orbit during STS-53. All of these factors were considered by the MIS-B design team to insure that MIS-B would be a significantly improved experiment in terms of space-made microsphere yield, of compliance to NASA specifications for hardware manifested in the Shuttle mid-deck, and of fabrication and assembly.

IV. METHODS OF APPROACH

Four experiments were incorporated into MIS-B. Once in the microgravity of space, the experiments produced pharmaceutical microspheres or control microspheres by using an ultrasonic spray nozzle to spray fluid into a cylinder with subsequent solvent removal. The difference between the four experiments was that two of them did not use the polymer/drug suspension employed in the other two. That is, the two experiments sprayed only polymer solution. From these experiments, we obtained control microspheres without microencapsulated drug to which comparisons can be made to drug-loaded microspheres. The other two experiments sprayed the same polymer/drug suspension to determine the reproducibility of the microencapsulation process, to increase the potential yield, and to have redundancy in the mission in case one of the experiments has operational problems.

All the experiments used ultrasonic spray nozzles to introduce microdroplets of polymer/drug/solvent or polymer/solvent mixtures into the hardening chambers. In microgravity, the microdroplets will float and, upon slow solvent removal, harden into microspheres. The polymer/drug/solvent mixture consisted of poly(DL-lactide-co-glycolide) (polymer), ampicillin anhydrate (drug), and ethyl acetate (solvent). The polymer/solvent mixture contained only poly(DL-lactide-co-glycolide) and ethyl acetate.

The four experiments were performed in groups of two. Each group of two experiments ran simultaneously for about 1¼ hours. After they are completed, the other group of two experiments ran simultaneously for the same duration. The total experimental operational time for MIS-B was about 2½ hours. We requested minimum activity of the Shuttle during the MIS-B experimental operations. During the solvent-removal period, we requested minimal operation of the Space Shuttle to prevent accelerations which could adversely affect the formation of the microspheres. These accelerations are typically caused by thruster firings performed to maintain orbital integrity.

After the Space Shuttle landed, we removed the microsphere product from the four hardening chambers of the MIS-B experiment. We then analyzed the structure of these microspheres. Because ampicillin anhydrate microspheres have been made on earth, the properties of the earth-made and space-made microspheres can be directly compared.

V. DESCRIPTION OF WORK

Major modifications to the design of the MIS-B hardware were needed from the design of MIS-A. The modifications involved correcting the causes of variances to NASA specifications found in MIS-A, improving the containment design, eliminating unnecessary subsystems that were incorporated in MIS-A, and redesigning the plumbing system of MIS-A. We also modified the MIS-B hardware in other ways that we determined would increase the probability of a successful mission. These modifications made the safety review process of MIS-B easier, made the prelaunch ground operations easier, improved the seal integrity of the primary and secondary containment systems, and improved the operation of MIS-B. Modifications which affect the MIS-B hardware as a whole are discussed first. Modifications concerning the separate systems of the MIS-B hardware are discussed afterward.

A. General Design and Fabrication

Two general design considerations were used in the design of MIS-B. First, MIS-A had exceedances to NASA middeck payload specifications in terms of weight, payload envelop, and electromagnetic interference. We examined these exceedances in MIS-A and corrected them in the design of MIS-B. Second, the yield of space-made microspheres was poor in MIS-A. In examining the results obtained from MIS-A, we modified the microencapsulation process in MIS-B with the goal of improving the yield of space-made microspheres.

1. Addressing the MIS-A Exceedances

Weight.

One of the first items which needed to be addressed in the design of MIS-B was the exceedances to NASA middeck payload specifications in both weight and payload envelop present in MIS-A. MIS-A exceeded the NASA weight specification by 22 lbs. (142 lbs. actual vs. 120 lbs. required). Therefore, we decided to address the weight problem first.

We accomplished weight reduction in the design of MIS-B by using both the elimination of unnecessary subsystems incorporated into MIS-A and by better design of the custom fabricated hardware such as structural supports and mounting brackets.

After reviewing the videotape from MIS-A, we decided that the data obtained from the videotape was not worth the cost in terms of electrical power, weight, and volume of incorporating the video recording system into the hardware. As a result, we decided not to use a video recording system in the MIS-B hardware. With the addition electrical power, weight, and volume available from removing the video recording system, more modifications to the MIS-B hardware could be accommodated. By removing the video recording system, less power was consumed by MIS-B.

Because of the spray dynamics generated by the ultrasonic spray nozzle, the electrostatic containment system on MIS-A was not strong enough to repel the charged microdroplets back towards the center of the hardening cylinder. As a result, the microdroplets collided with the nylon mesh in the hardening cylinders of MIS-A which functioned to separate the molecular sieve absorbent from the drying area. This was the major reason for the poor yield of space-made microspheres in MIS-A.

Two phenomena were primarily responsible for the low yield of space-made microspheres in MIS-A. These two phenomena were the forcing of the polymer/drug suspension to the walls of the hardening cylinder by the spray dynamics and the wettability of nylon for the polymer/drug suspension. Because of the strength of these two phenomena, the electrostatic containment field in one of the hardening cylinders was not strong enough to keep the polymer/drug suspension droplets away from the nylon mesh. Although electrostatic containment may prove in the future a valuable method of controlling the polymer/drug suspension spray in microgravity, we eliminated the electrostatic containment system from the MIS-B hardware. Other modifications to the hardware were made to provide the necessary means of controlling the polymer/drug suspension spray and increasing yields. These modifications included increasing the volume of the hardening chamber, constructing the hardening cylinder from material nonwettable to the polymer/drug suspension, and finding a method to move the polymer/drug suspension spray away from the ultrasonic spray nozzle.

In summary, the subsystems of MIS-A that we determined were unnecessary in MIS-B were:

- Video recording system
- Fiber optic lighting system
- Programmable logic controller (replaced with a custom-designed, hardwired control circuit)
- Electrostatic containment system

With the elimination of these subsystems, a significant weight reduction was possible with MIS-B. In addition to these subsystem eliminations, we chose a different design team for MIS-B than was used for MIS-A. This new design team at Dynetics, Inc., had access to the latest computer-aided design programs. This enabled the design of the custom-fabricated hardware to be precisely controlled so that the minimum weight possible for structurally sound hardware could be realized. In addition, detailed layout of the MIS-B components with the computer could be performed insuring full utilization of the payload envelop available to MIS-B.

Because of these reasons and to increase the redundancy built into the experiment, we decided to increase the number of experiments from two on MIS-A to four on MIS-B. Two of the experiments sprayed a polymer/drug suspension while the other two were control experiments in which only the polymer solution was sprayed.

Payload Envelop

MIS-A exceeded NASA middeck payload specifications for payload envelop. The x-axis dimension for MIS-A was 0.875 in. too long. (Note: The x-axis for middeck payloads is oriented from the wire trays onto which the payloads are mounted into the middeck common area.)

Because of the changes to the control system and the incorporation of active cooling into the MIS-B hardware, the outer cover and control panel were redesigned. During this redesign, we took advantage of the opportunity to shorten the x-axis length of the outer cover to conform to NASA specifications for middeck experiments. We used the outer cover from the MIS-A backup model for MIS-B. To accommodate the design changes, we cut the front panel off the MIS-A outer cover and removed enough of the side panels to achieve the 0.875 in. length reduction in the x-axis. Then, we welded a new, redesigned front panel onto the shortened side panels. Incorporated into the new front panel are inlet and outlet ports for the active cooling and a new, redesigned control panel.

The new control panel attaches in a deeper well on the front panel of the outer cover. On MIS-A, the locking toggle switches protruded past the edge of the front panel. Although this did not present a safety concern to NASA, we decided for MIS-B to deepen the well in which the control panel is located to totally contain the locking toggle switches. Besides the main power fuse, the main power switch, and the experimental start switch, the new control panel contains more indicator lamps to display the operating status of the four experiments, an additional locking switch to activate the active cooling system, and an additional fuse for the active cooling power circuit.

Electromagnetic Interference

MIS-A needed a variance because of exceedances to NASA payload specifications for conducted electromagnetic interference. Electromagnetic interference generated by MIS-B was less than that generated by MIS-A. This is because the main sources of electromagnetic interference are power converters and video equipment. We removed the video equipment and the electrostatic containment system which possessed a power converter from MIS-B. The only sources of electromagnetic interference on MIS-B are the ultrasonic spray nozzle power supplies and the main power converters. In addition, we kept the main power circuitry that was used in MIS-A. However, a variance for MIS-B similar to that granted to MIS-A to exceedances in conducted electromagnetic interference was necessary due to the electromagnetic interference generated by the ultrasonic spray nozzle power supply.

2. Active Cooling

Although we reduced the power consumption of the MIS-B hardware by eliminating the video recording system, MIS-B could still generate an unacceptable amount of heat during operation due to the longer operating time. Therefore, we designed MIS-B with active cooling.

During the operation of MIS-A on-orbit, the temperature inside the hardening cylinders reached almost 30 °C after 4 h. Although 30 °C was acceptable for the operation of MIS-A, this temperature was the upper limit of what is tolerable in the experiment. The MIS-B hardware operated for a shorter time period (2½ hr); however, two of the ultrasonic spray nozzles and the syringe pumps operated for the entire operating time of MIS-B as opposed to only 5 min for MIS-A. Active cooling of the MIS-B hardware was necessary to prevent operating temperatures from exceeding 30 °C.

Active cooling involves the use of a fan to cool the operating hardware. In microgravity, convective cooling does not occur because the density difference between hot and cold air is not present. Therefore, hot air from around operating equipment in microgravity will not rise and be replaced with cooler air. In equipment without active cooling systems, heat generated by operating equipment must be dumped passively. Passive cooling occurs by the conduction of heat from the hot metal components of the operating equipment to cooler metal parts of the Shuttle. For low heat loads, passive cooling is adequate. But, for continuously operating equipment, heat loads may overwhelm the heat conduction capacity. Therefore, fans are used to generate convective air currents which allow for heat to be dumped convectively.

3. Polymer Solvent Change

In MIS-A, we used methylene chloride as the solvent for the polymer. Methylene chloride is a excellent solvent for poly(DL-lactide-co-glycolide). However, methylene chloride is somewhat toxic. Therefore, we decided to switch the polymer solvent from methylene chloride to ethyl acetate. Ethyl acetate is less toxic than methylene chloride and, therefore, a more readily accepted pharmaceutical solvent. However, ethyl acetate is flammable whereas methylene chloride is not.

An added benefit of switching to ethyl acetate was that ethyl acetate has a much higher boiling point. This effects both safety and operational issues associated with MIS-B. With regards to safety, less pressure will build up inside the primary and secondary containment systems of MIS-B because ethyl acetate will not vaporize as readily as methylene chloride at the maximum design temperature for MIS-B under a credible, two-fault scenario.

With regards to operational issues, a polymer/drug suspension made with ethyl acetate can be sprayed through an ultrasonic spray nozzle at a much slower rate than a similar polymer/drug suspension made with methylene chloride. This is because the ultrasonic spray nozzle heats up when operating. When methylene chloride is used as the polymer/drug solvent, some of it is vaporized at the nozzle tip. This requires that the flow rate of polymer/drug suspension through the nozzle be fast enough to compensate for this vaporization and to keep the nozzle tip cool. In addition, the polymer concentration can not be too high because the viscosity of the fluid being sprayed through an ultrasonic spray nozzle has a direct effect on the spraying efficiency. As a result, polymer concentrations in methylene chloride had to be kept low so that the viscosity increase associated with the vaporization of a portion of the methylene chloride solvent would not adversely affect spraying efficiency.

Because ethyl acetate will not vaporize as readily as methylene chloride, the flow rate of polymer/drug suspension made with ethyl acetate through the ultrasonic spray nozzle could be much slower than that needed if methylene chloride is used as the solvent. In addition, higher polymer concentrations are possible for the same reason. These two effects, slower spraying rate and higher polymer concentrations, are what we determined to be important in increasing the yield of space-made microspheres. A slower spraying rate will allow for a better utilization of the drying volume available in the hardening chamber. A higher polymer concentration will allow for more polymer and drug to be incorporated into the amount of solvent which can be accommodated inside the payload envelop volume that NASA has given for MIS-B.

In switching from methylene chloride to ethyl acetate, we found that the solvent adsorbent needed to be changed. Ethyl acetate is not efficiently adsorbed into type A molecular sieves which were used in MIS-A. After testing many different types of adsorbents, we found that silica gel performed the best. We used the silica gel (8- to 12-mesh beads).

4. Plumbing System

We also designed new syringe pumps for the MIS-B hardware. Because of the syringe-pump modifications necessitated by different operating parameters for MIS-B as opposed to MIS-A, we redesigned the syringe pumps and made substantial improvements to the pump design. The operating parameters for MIS-B involved spraying only half the polymer/drug suspension per hardening chamber and spraying at a much slower flow rate. The new design incorporated many of the same features found in the syringe pumps used in MIS-A. However, the new pumps were lighter, possess simpler construction, and incorporate a more efficient stir motor. The new pump design also incorporated modifications to address concerns raised by NASA regarding the MIS-A pump design. In addition, each pump was integrated into its respective hardening cylinder structure. That is, all of the components are mounted on a common manifold block. Holes were drilled through the manifold block to connect the pump components together. And, the components were arranged to provide for the shortest pathlength between them. The components attached to the manifold block were the syringe pump, the mixing motor, the solenoid valve, the safety by-pass, and the ultrasonic spray nozzle. The complete plumbing unit was mounted directly on the top part of the hardening chamber.

5. Hardening Chamber Air Recirculation

To improve the circulation of the polymer/drug suspension droplets sprayed into the hardening chamber, we installed a piezoelectric fan inside the hardening chamber. The fan is situated at the bottom of the hardening chamber and direct a gas stream into a duct. The duct is situated on the side of the hardening chamber interior and ends at the ultrasonic spray nozzle. The flow rate generated by the fan is very slow; we anticipate only a small number of complete turnovers of backfilling gas in the hardening chamber.

The purpose for installing the piezoelectric fan in the hardening chamber was to help disperse the polymer/drug suspension droplets more evenly throughout the hardening chamber volume. A

major problem with MIS-A was that the polymer/drug suspension droplets were not adequately dispersed throughout the available hardening chamber volume. As a result, microsphere yields were low.

6. Primary and Secondary Containment Systems

In the process of designing the primary and secondary containment systems for MIS-B, we found that the original MIS-B design of the containment systems would be too difficult to incorporate structurally into the MIS-B hardware. We modified the containment system design to alleviate this problem. The new design of the primary and secondary containment systems involved using separate primary and secondary containments for each hardening chamber.

Each hardening cylinder had its own primary and secondary containment system. By designing each hardening cylinder with its own primary and secondary containment system, smaller containment volumes resulted. With smaller containment volumes, less pressure could build up under a credible two-fault failure scenario. In addition, we found that the individual containment systems could be packed into a tighter volume.

The primary containment involve the hardening chamber and the plumbing system. This was similar in design to the primary containment system for MIS-A. The secondary containment involved a cylindrical sleeve which fits over the bottom part of the hardening chamber and a cover which fits over the top part of the hardening chamber and the plumbing system.

In addition, we constructed the hardening chamber from aluminum. This is different from MIS-A in which the hardening cylinder was constructed from Nylon. Using aluminum allowed for a stronger, lighter hardening chamber for MIS-B.

After examining the MIS-A hardware post-flight, we found most of the polymer/drug suspension dried on the nylon mesh. In additional, we found that the nylon mesh had a continuous film of polymer/drug suspension for only about 4 inches down the hardening cylinder. As the axial distance increased down the hardening cylinder away from the ultrasonic spray nozzle, we found less and less polymer/drug suspension dried on the nylon mesh. We modified the inside surfaces of the MIS-B hardening chambers to make them nonwettable to the polymer/drug suspension. A nonwettable surface for the polymer/drug suspension could be formed by coating the inside surface of the hardening chamber, the air ducts, and the adsorbent container with a fluorosilicone coating (Dow Corning 94-003 Dispersion Coating).

7. Control System

Because the operation of MIS-B was inherently simpler than the operation of MIS-A, the control system for MIS-B was not as complicated as for MIS-A. That is, we eliminated the computer used to control MIS-A and replaced it with a hardwired control circuit. By hardwiring the control circuit in MIS-B, less electrical power and volume was needed when compared to the computer used

in MIS-A. In addition, the layout of the control panel components (switches, indicator lamps, receptacles, etc.) was optimized for space.

8. Backfilling Gas

Gaseous nitrogen was used to backfill the primary and secondary containment systems. However, during the preflight ground operation, we pressurized the containment systems with helium. A helium leak detector was then used to locate and quantify leaks in the containment systems. This allowed for a faster and more accurate structural and seal integrity tests to be performed during hardware verification and during the prelaunch ground operations. Structural and seal integrity tests for MIS-A were performed using a pressure decay method. A pressure-decay test take a long period of time to perform and is extremely vulnerable to changes in temperature. Using a helium leak detector speeded up the verification tests without sacrificing accuracy.

B. Design and Fabrication of MIS-B Hardware Systems

The section below is divided into six sections. Each section describes the design and fabrication of each system of the MIS-B hardware. The systems of the MIS-B hardware were designed with flexibility to accommodate future experimental design changes. The systems for the MIS-B hardware are:

- Control Subsystem
- Active-cooling Subsystem
- Ultrasonic Spray Nozzle Subsystem
- Pumping Subsystem
- Hardening Chamber Subsystem
- Electrical Subsystem

We designed the MIS-B hardware with three levels of containment to satisfy NASA safety requirements. The first level of containment consisted of hardening chambers and the pumping system for the polymer/drug/solvent mixture. The second level of containment was an aluminum box which completely enclosed the first level of containment - the hardening chambers and the pumping system. The third level of containment is another aluminum box which completely encloses the first and second level of containment along with the remaining components of the MIS-B hardware. Located on this outer containment box are the switches and indicator lights required for operation of the MIS-B hardware.

The first and second containment level were sealed against chemical leakage through the use of chemically-resistant O-rings in the seams between the structural components. The third containment level is not sealed against chemical leakage. It functions primarily to contain any internal component of the MIS-B hardware which could accidentally break free during liftoff, landing, or an emergency maneuver.

1. Control Subsystem

The control subsystem is used to sequence the various components of the MIS-B subsystems and the four experiments contained within MIS-B. The control subsystem consists of the following components.

- ✦ Control Panel
- ✦ Microstep Motor Indexers (4)
- ✦ Control Boards (2)

Control Panel

The control panel for MIS-B is located on the front panel of the MIS-B outer cover. On the control panel are three switches, four 5-A fuse holders (two active, two spares), one power cable connector, one temperature monitor display, and seven indicator lamps.

One of the three switches activates the active-cooling subsystem. The other two operate the MIS-B experiments. One of these two switches is the main power switch; it is a locking switch. The other switch is a push-button switch which will provide an impulse signal to a latch on Control Board 1. The impulse signal will also cause a "go" command to be sent to the microstep motor indexers which initiates the program resident in non-volatile memory devices on the indexers. In summary, the switches have the following functions.

- ✦ Active-cooling Switch - Activates the active-cooling subsystem independent of the main power switch. The switch is a locking switch.

- ✦ Main Power Switch - Activates main power to MIS-B. Components that will be powered-up at this time will include the dc-to-dc power converters, the power indicator lamp, the microstep motor indexers, and the control boards. The switch is a locking switch.

- ✦ Experiment Start Switch - Provides an impulse signal to initiate the indexers. The switch is a push-button.

The fusing for MIS-B consists of four fuses - two active and two spares. One set of active/backup fuses is used in the main power circuit. The other set is used in the active-cooling subsystem circuit.

Microstep Motor Indexers and Control Boards

The MIS-B control electronics subsystem governs the timing and implementation of the processes involved in the operation of MIS-B. The central components of the system consist of two control boards and four indexers. The control boards were designed and developed by Dynetic, Inc.,

and the indexers were purchased from Technology 80, Inc. Both the control boards and indexer work together to control the operation of MIS-B. However, the control program resides in non-volatile memory on the indexer boards.

The control boards are 5.75-in by 5.25-in, double-sided, printed circuit cards. These cards each house 14 integrated circuits, two DIP switches, two momentary switches, and five multi-pin connectors. Various resistors, diodes, and capacitors are also located on the cards. The indexers are 3.0-in by 2.75-in by 1.20-in modules in which is mounted a single printed circuit card for three indexers or two printed circuit cards for the fourth. The second printed circuit card on the fourth indexer provides RS-232 interfacing with a personal computer. The program code used by these indexers is stored in non-volatile memory devices; therefore, no batteries are required by the indexers. In fact, no batteries are required for any component of the MIS-B control electronics.

The control boards govern the actuation of many of the events in the operation of MIS-B. They also provide drive currents for certain events governed by the indexers. The control boards accept the Experiment Run Switch command and control the operation of the run indicator lamp on the control panel, the ultrasonic power supplies, and the solenoid valves. The indexers primarily govern the operation of the stepper-motors found the syringe pumps of MIS-B. They also control the operation of the piezoelectric recirculation fans, the ultrasonic power supply relays, the mixing motors, and the experiment-complete indicator lamps.

Although we are using the same stepper motors that we used in MIS-A, we are changing to the microstep motor drivers to produce a smoother, more controllable motion to the syringe pump. This, in turn, will produce a more uniform spray from the ultrasonic spray nozzles.

2. Active-cooling Subsystem

Although we did not use active cooling in MIS-A, we incorporated an active-cooling subsystem into MIS-B. This is because we planned to operate the ultrasonic spray nozzle and pumping subsystems for a much longer period of time in MIS-B than in MIS-A. From the results of the MIS-A flight aboard STS-53, we found that the internal temperature increased to about 30 °C during the initial operation and, then, decreased. Because of the longer operating period of the spray nozzles and pumps in MIS-B, an active-cooling subsystem would be necessary to maintain a constant internal temperature.

The active-cooling subsystem consists of an inlet port, an outlet port, and a fan. The fan is a conventional turbine cooling fan. The circuitry for the active-cooling subsystem is independent from the MIS-B experiment circuitry and has its own fusing. The inlet and outlet ports is located on the front panel of the MIS-B outer cover. Middeck air is pulled into MIS-B and circulate inside the outer cover. Then, the air is exhausted into the middeck. No air exchange occurs inside the secondary or primary containment levels.

Because most of the electronic components are located between the outer cover and the secondary containment level, most of the heat generation occurs in this volume. Therefore, most of the heat load generated by MIS-B can be dissipated by circulating middeck air through this volume.

The active-cooling subsystem can be activated independently of the main power to the MIS-B experiments as long as the MIS-B power cable is connected to the Shuttle power bus. Activation of the active-cooling subsystem is accomplished by a switch located on the MIS-B control panel.

3. Ultrasonic Spray Nozzle Subsystem

The ultrasonic spray nozzle subsystem used in MIS-B are the same as used in MIS-A except that two subsystems are used in MIS-B.

Each of the four experiments has a dedicated ultrasonic spray nozzle. The ultrasonic spray nozzle takes the stream of polymer/drug suspension supplied by the pumping system and sprays small diameter droplets into the hardening chamber. The spray nozzle operation is similar to an acoustical speaker. That is, an ultrasonic frequency signal is generated by the ultrasonic power supply. This signal drives the piezoelectric crystal inside the body of the spray nozzle. This, in turn, vibrates a titanium nozzle through which the polymer/drug suspension flows. The nozzle is designed to have a resonance point for the ultrasonic frequency signal at its end. As a result, fluid flowing over the end of the nozzle is vibrated. If this vibration is strong enough, the fluid is sheared into droplets and propelled off the nozzle end. However, the linear velocity at which the droplets are propelled is much slower than for conventional two-fluid or rotary-head spray nozzles. The low velocity spray makes the ultrasonic spray nozzle ideal for microgravity applications.

The ultrasonic spray nozzle subsystem is custom-designed so that two ultrasonic spray nozzles are powered from one ultrasonic spray nozzle power supply. Therefore, two ultrasonic spray nozzle power supplies are used in MIS-B. Both ultrasonic spray nozzle power supplies are located on the electronic tray. A relay is used to switch the operation of the power supply from one ultrasonic spray nozzle to the other. Each power supply has its own relay. The operation of these relays is controlled by the control subsystem. Coaxial cables connect the power supplies to the ultrasonic spray nozzles. Coaxial pass troughs are used to maintain containment of the secondary containment level.

Ultrasonic spray nozzles were chosen for the MIS-B experiment because they can produce a fine spray of 40- to 50-μm microdroplets. Additional, the spray produced by these nozzles has low initial velocity. Because of this low initial velocity, the microdroplets produced by these ultrasonic spray nozzles should have stopping distances at normal air pressure within the size constraints of the hardening chambers. However, results of MIS-B operation indicate that the hardening chamber length was not long enough to accommodate the anticipated stopping distances. Streamlining of the spray as it came off of the nozzle tip may have been responsible for the observed increase in stopping distances.

The ultrasonic spray nozzles were purchase from Sono-tek Corporation (Poughkeepsie, NY). Sono-tek modified their commercial spray nozzle system so that their nozzles would be more easily adapted to the MIS-B hardware. These modifications reduced the power requirements, the volume, and the weight of the ultrasonic spray nozzle system. These modifications included changing of the power source requirements from 120 Vac to 28 Vdc so that the spray nozzles could be powered directly from the Shuttle power supply. And, a second spray nozzle control module was added to the power supply so that one power source could power both spray nozzles.

By examining the spray pattern produced by the ultrasonic spray nozzle, we were able to determine the average axial and radial velocity of microdroplets of the polymer/drug/solvent mixture off the ultrasonic nozzle tip. For a 50-μm microdroplet, we calculated that the average radial velocity off the ultrasonic spray nozzle tip was about 0.07 cm/sec. At this average radial velocity, the microdroplet will stop moving due to air resistance in less than 1 cm. For 50-μm microdroplets, the diffusional velocity is extremely small.

The calculated average axial velocity for a 50-μm microdroplet is about 0.20 cm/sec. At this average axial velocity, the microdroplets will stop moving due to air resistance in about 3 cm. In practice, the ultrasonic spray nozzle imparts a wide range of axial velocities to the microdroplets. And, convective air currents generated by the microdroplet spray will increase the average stopping distance of the microdroplets. However, in the spraying experiments conducted on earth, we did not measure a spraying distance greater than 16 cm. Therefore, the length of the hardening chamber should have been sufficient to accommodate the average stopping distance of most, if not all, of the microdroplets sprayed through the ultrasonic spray nozzle.

4. Pumping Subsystem

The pumping subsystem is used to deliver the polymer/drug suspension to the ultrasonic spray nozzles. Each hardening chamber has a complete pumping subsystem for a total of four pumping subsystems in MIS-B. The subsystem consists of a custom-built syringe pump with a built-in agitator. Because we custom-designed the pump manifold, no plumbing fittings (tees, elbows, etc.) are needed. All of the plumbing is internal to the pump manifold. Therefore, the probability of leaks occurring in the pumping subsystem is highly unlikely. The rest of the pumping subsystem consists of a solenoid valve controlled by the control subsystem, inlet and outlet ports, and a safety bypass. All of these other components are fitted onto the pump manifold.

The plunger in the syringe pump moves by a stepper motor. The stepper motor is controlled by microstep motor driver of the control subsystem. Polymer/drug suspension is charged into the syringe pump during the preflight ground operations. The pumping system delivers polymer/drug suspension to the ultrasonic spray nozzle located at one end of the hardening chamber. In case the solenoid valve does not open or the ultrasonic spray nozzle becomes clogged, a relief valve located in the safety bypass opens and allows polymer/drug suspension to bypass the solenoid valve and the ultrasonic spray nozzle. The outlet for the safety bypass is in the hardening chamber. This bypass prevents a breach of primary containment in the case of a solenoid valve failure or a plumbing clog.

5. Hardening Chamber Subsystem

Each experiment has a dedicated hardening chamber subsystem. The hardening chamber is constructed from 6061-T6 aluminum. The inside surface of the hardening chamber is coated with a fluorosilicone coating (Dow Corning Type 94-003 Dispersion Coating). This coating prevents the microdroplets of polymer/drug suspension from sticking to the inside surface of the hardening chamber.

The hardening chamber is constructed as a cylinder which is closed at one end. The open end is attached to a mounting flange. Also attached to this mounting flange is a container for the solvent absorbent. A silica gel absorbent is used to absorb the solvent for the polymer/drug suspension.

A piezoelectric fan is located in the bottom part of the hardening chamber at the end opposite the ultrasonic spray nozzle. The fan provides circulation of the polymer/drug suspension spray. This prevents the accumulation of polymer/drug droplets in front of the ultrasonic spray nozzle and moves the microdroplets throughout the working volume of the hardening chamber. A major problem in MIS-A was that the microdroplets did not travel down the length of the hardening chamber.

Associated with the piezoelectric fan is a circulation conduit that is located along the side of the bottom part of the hardening chamber. At one end of the circulation conduit is the piezoelectric fan. The other end terminates near the ultrasonic spray nozzle. Sealed pass-troughs on the hardening chamber mounting flange provide electrical connections to the piezoelectric fan. To prevent ground looping, the piezoelectric fan and its driver board are isolated from the MIS-B chassis. The electrical connections for the piezoelectric fan are then ganged with the other electrical connections for the motors and valves inside the secondary containment through another sealed pass-through on the bottom part of the secondary containment.

6. Electrical Subsystem

The electrical subsystem contains the wiring harness, the power supplies, and other electronic components. These electronic components are needed to condition the electrical power from the Shuttle power bus, to shield the Shuttle from electromagnetic interference generated by MIS-B, and to sequence the powering up of the individual components of the MIS-B experiment so as to spread the start-up current flow over a longer period of time. This design was used to comply with NASA's transient turn-on voltage and amperage specifications.

The electrical leads for the wiring harness are all 22-gauge with Teflon® insulation rated to 200 °C. Two dc-to-dc power supplies are necessary to convert the 28 Vdc power from the Shuttle power bus to 12 Vdc and 5 Vdc. These voltages are needed to power some of the components of MIS-B.

Because of the ultrasonic power supplies and the dc-to-dc power supplies, MIS-B generated unacceptable levels of conducted electromagnetic interference. Conducted electromagnetic

interference is that interference which is conducted through the power leads of MIS-B into the Shuttle power bus. To reduce the conducted electromagnetic interference, three strategies are used. First, capacitors are connected across the three power leads for MIS-B. Across the ground-to-power and the ground-to-return leads, 0.1 μF capacitors are used. Across the power-to-return leads, a 1.0 μF capacitor is used. Second, the power and return leads are counter wound around to toroidal iron core. This causes some of the interference to destructively combine and to cancel each other. Third, the power and return leads are connected to a radio frequency interference filter. Even with these strategies, MIS-B had a minor exceedance in conducted electromagnetic interference for which a variance was granted by NASA.

To enable MIS-B to be disassembled easily, we incorporated in-line connectors in all wiring harness trunks that connect different subsections of MIS-B. For example, in-line connectors are present in the two wiring harness trunks from the control panel to the electronics board. They are present in the wiring harness trunks which connect the electronics board to the individual experiments. Finally, they are present inside the secondary containment to enable easy removal of the secondary containment box.

C. Containment Levels for MIS-B

1. Overview

Due to the potential toxicity and flammability of the solvent (ethyl acetate) used in the experiments, the MIS-B payload hardware was designed with double chemical containment. With the amount of ethyl acetate used in the MIS-B experiment (about 20 mL/hardening chamber, 4 chambers total), a Level 1 toxicity was indicated by NASA personnel.

The containment levels have been designated primary and secondary. Four primary containment levels are present in MIS-B. Each primary containment level consists of a hardening chamber, an ultrasonic spray nozzle, and a pumping subsystem. The four hardening chambers, the four ultrasonic spray nozzles, and the four pumping subsystems which comprise the primary containment levels are not connected.

Four secondary containment levels are present in MIS-B. Each secondary containment level consists of a top housing which surrounds a hardening chamber and a bottom housing which encloses the pumping subsystem and the ultrasonic spray nozzle. The four secondary containment levels are not connected.

Electrical service to the components of the hardening chamber and pumping subsystems is accomplished by using appropriate bulk-head pass throughs.

2. Primary Containment Level

The primary containment level is essentially the volume in which the actual experiments are performed. Because of the presence of ethyl acetate in the experiments, it is necessary to seal this level. The three components of each primary containment level are the hardening chamber, the ultrasonic spray nozzle, and pumping subsystem.

Hardening Chamber

The hardening chamber is a cylinder with a welded end piece on one end and the other end open. The open end has a face plate so that the hardening chamber can be attached to the mounting flange. A hemispherical end piece is welded to the other end of the cylinder. The hardening chamber cylinder body, end piece, and face plate are constructed from 6061-T6 aluminum.

The hardening chamber cylinder body has dimensions of 10.913 in. length and 6.480 in. inside diameter. It is constructed from 0.125-in. thick aluminum. The hemispherical end piece has a radius of 10.310 in. and is also 0.125-in. thick. This makes the total length of the hardening chamber 11.715 in. A locator hole is situated in the center of the end piece to provide a positive fit into the hardening chamber support bracket located in the secondary containment top cylinder. The end piece also has three feet to provide additional support for the hardening chamber to the secondary containment top cylinder.

The hardening chamber face plate is welded to the open end of the hardening chamber cylinder body. It is designed so that the mounting holes are to the inside of the cylinder body. Twelve helicoil inserts are located in the face plate for bolting the face plate and, subsequently, the hardening chamber to the mounting flange. An O-ring groove is cut in the face plate to accept an ethylene-propylene-diene monomer (EPDM) O-ring. The EPDM O-ring provides chemical seal integrity between the hardening chamber face plate and the mounting flange.

Silica gel is used to absorb the polymer solvent (ethyl acetate) during the experiment. The silica gel is in the form of 3-mm beads (Aldrich Chemical Company, Inc.;Catalog No. 25,562-9). During the experiments, the silica gel beads are contained within a housing attached to the bottom side of the mounting flange. Therefore, the silica gel bead housing will protrude into the hardening chamber cylinder body. The silica gel bead housing has a volume of about 15 cubic inches. This volume is sufficient to hold almost 200 g of silica gel beads.

The silica gel bead housing is in the form of an annulus situated around the ultrasonic spray nozzle. In fact, the housing provides additional support to the ultrasonic spray nozzle. Because of the support given to the ultrasonic spray nozzle, the housing has two O-ring grooves that accept EPDM O-rings. The O-rings maintain primary containment. One EPDM O-ring provides a seal for the ultrasonic spray nozzle. The other EPDM O-ring provides a seal between the inside edge housing and the mounting flange. The outside edge of the housing does not need an O-ring to maintain primary containment. The hardening chamber face plate O-ring serves this purpose.

Pumping Subsystem

The pumping subsystem is other integral part of the primary containment level. It consists of a syringe pump, a pump housing, a solenoid valve, an ultrasonic spray nozzle, and a safety bypass. All five components of the pumping subsystem are contained in or attached to the pump housing. The pump housing is constructed from 6061-T6 aluminum. It is rectangular block with dimensions of 2.800 in. in length, 2.065 in. in width, and 2.250 in. in height.

The pump housing is a manifold to which the stepper motor for the syringe pump is attached. The body of the syringe pump is incorporated into the pump housing. Inlet and outlet ports for charging the syringe pump with polymer/drug suspension are tapped into the pump housing and connect to the syringe pump body. The syringe pump outlet is tapped through the pump housing and leads to the solenoid valve. At the outlet of the solenoid valve, another hole is tapped which leads to the ultrasonic spray nozzle. The ultrasonic spray nozzle inlet tube is press-fit into this hole. The syringe pump outlet also branches to the safety relief valve.

The safety relief valve is preset to open once 40 to 80 psid of pressure is generated by the syringe pump. Upon testing, the cracking pressure for the safety relief valves was found to be about 65 psid. Once the safety relief valve opens, the polymer/drug suspension bypasses the ultrasonic spray nozzle and the solenoid valve and feeds directly to the hardening chamber. Therefore, no breach of primary containment can occur if the solenoid valve fails to open or a clog occurs in the plumbing lines to the ultrasonic spray nozzle.

3. Secondary Containment Level

There are two components of the secondary containment level: a cylindrical housing which surrounds the hardening chamber and a housing which encloses the pumping subsystem and ultrasonic spray nozzle. Both secondary containment level housings attach to the mounting flange.

Each primary containment level has a dedicated secondary containment level. Therefore, there are four secondary containment levels. The primary and secondary containment levels for two experiments are mated together on one mounting flange for structural integrity. The mounting flange is then attached to suitable structural supports inside the outer cover.

The cylindrical housing which surrounds the hardening chamber is constructed from 6061-T6 aluminum. The cylinder body is 11.038 in. in length and has a 7.300 in. inside diameter. Similar to the hardening chamber, the secondary containment has a face plate and an end piece welded to opposite ends of the cylinder body. Both the face plate and end piece are constructed from 6061-T6 aluminum. The face plate has twelve helicoil inserts for bolting it to the mounting flange. However, the face plate is designed so that its mounting holes are on the outside of the cylinder body as opposed to the hardening chamber face plate. An O-ring groove is cut into the face plate which can accept an EPDM O-ring. This provides chemical containment for the secondary containment level.

The end piece is shaped from 0.78-in. aluminum circular plate. Its thickness is no less than 0.10 in. The outer axial edge of the plate is rounded to a 1.312-in. radius. Situated in the middle of the end piece is a locator tab. The locator tab fits into the locator hole situated on the outside surface of the hardening chamber end piece. An inlet port for backfilling the secondary containment level is also located on the end piece.

For the bottom part of the secondary containment level, a rectangular housing is used. The housing is 6.50 in. in length and 7.50 in. in width. The housing is constructed from 6061-T6 aluminum and was manufactured by Zero Enclosures (North Salt Lake, Utah). The housing is welded to flange so that it can be attached to the mounting flange. The housing flange has 22 mounting holes for attaching the housing to the mounting flange. An O-ring groove is cut into the housing flange. Chemical containment is achieved when an EPDM O-ring is placed in the groove and the housing is bolted to the mounting flange.

4. Mounting Flange

The mounting flange is an integral part of both the primary and secondary containment levels. The mounting flange is the point of attachment for the hardening chamber cylinder body, the silica gel bead housing, and the secondary containment level cylinder on one side and the pumping subsystem and the secondary containment level top housing on the other.

The mounting flange is constructed from 6061-T6 aluminum plate that is 0.50 in. thick. It is 8.13 in. in width and 16.50 in. in length. These dimensions of the mounting flange provide sufficient area to attach the complete primary and secondary containment levels for two experiments. The mounting flange was designed in this manner to provide additional structural support for the primary and secondary containment levels. It also reduced the volume requirements for structural supports in the MIS-B hardware compared to separate mounting flanges for each experiment. Finally, preflight ground operations were easier by having two hardening chambers mated through a single mounting flange than if all four hardening chambers were mated together.

5. Outer Cover/Mounting Panel

The outer cover/mounting panel provides debris containment for the rest of the components of the MIS-B payload. It is not sealed but functions as a containment against internal components which might break free during liftoff, landing, or an emergency maneuver. The mounting panel completes the enclosure and provides a structural support for the electronics tray and the secondary containment level. The mounting panel is bolted to a NASA-supplied double adapter plate at the four corner bolt locations. Located on the front panel of the outer cover are the inlet and outlet ports for the active-cooling subsystem and the control panel. Also located on the front panel is the control panel for MIS-B. The receptacle for the 28 Vdc power cable is located on the control panel along with the switches and indicator lamps for the MIS-B experiments.

The outer cover for the MIS-A backup model was used to construct the outer cover for MIS-B. The MIS-A outer cover was modified to accommodate the active-cooling subsystem and the new control panel. The length of the MIS-A outer cover was also reduced by 0.875 in. to be in compliance with NASA's payload envelope restrictions for middeck payloads.

The payload envelope dimensions for MIS-B are 19.43 in. x-axis, 18.00 in. y-axis, and 21.75 in. z-axis (coordinate system per NSTS 21000-IDD-MDK). These payload envelope dimensions do not include the NASA-supplied double adapter plate and payload mounting panels. Both the outer cover and MIS-B mounting panel are constructed from 6061-T6 aluminum. The MIS-B mounting panel is 0.50 in. thick. To reduce the weight of the MIS-B mounting panel, half the thickness of the panel was removed in areas deemed insignificant for structural integrity. Six areas were identified and the panel thinned in these locations.

VI. RESULTS

A. First Preflight Ground Operation

The first preflight ground operation was performed on Cape Canaveral Air Force Station by members of the MIS-B ground operations team which included representatives from the U.S. Air Force integration office, Aerospace Corp., Muniz Engineering, Inc., and Southern BioSystems, Inc. (SBS). We performed the first preflight ground operation on May 29, 1995, through June 2, 1995, to support a tentative launch of STS-70 on June 8, 1995. The MIS-B hardware was successfully preflighted during this operation and received NASA flight certification. The hardware was turned over to NASA for installation in the Orbiter on June 2, 1995. No problems occurred in installing the hardware in the Orbiter or testing the electrical power circuits.

The June 8, 1995, launch of STS-70 was scrubbed primarily due to holes punched by woodpeckers in the insulation covering the external fuel tank. After the launch scrub, the MIS-B hardware was removed from the Orbiter and returned to SBS.

During these prelaunch ground operations, we encountered some problems associated with verifying seal integrity to leaks, stalling of the stir motors, and minor deviations in the indexer program. Because of the launch scrub, we decided to investigate these problems and fix them before the next launch opportunity.

1. Mounting Flanges

We identified a potential leak problem with the mounting flange to which the hardening chambers and secondary containment vessels are attached. In addition to having an inaccessible bolt, the mounting flange had been lapped. The lapping procedure produces uniform scratches over the surface of the metal. The lapped surface of the mounting flanges increased the possibility of leaks occurring in the hardening chamber/mounting flange and secondary containment vessel/mounting flange seals. Therefore, we constructed new mounting flanges to correct for the bolt inaccessibility and to produce a smoother surface finish. Upon receiving the new mounting flanges, we discovered that the bolt-hole pattern was cut incorrectly into the mounting flange. And, with no time before the next launch opportunity to have the mounting flanges remade, we decided to install the new mounting flanges into the MIS-B hardware. The incorrect bolt-hole pattern resulted in no improvement in the bolt inaccessibility. However, the mounting flanges did have the smoother surface finish and, because of this characteristic, we decided to install the new mounting flanges in MIS-B.

2. Pump Bushings

During the first prelaunch ground operations, we experienced some problems with the bushings which form part of the seal for the stir motor shaft. These bushing had been constructed from Delrin polymer. Apparently, ampicillin anhydrate particles from previous tests of the plumbing system associated with the polymer bushings and affected the free rotation of the stir motor shafts. Because the ampicillin anhydrate does not dissolve in the polymer solvent, particles of ampicillin anhydrate may have gotten stuck between the mix motor shaft and the bushing. Because Delrin is a hard polymer, the particles caused the mix motor shaft to seize. Therefore, we decided to replace the Delrin bushings with brass. Brass is a more malleable material than Delrin, brass bushings may be more tolerant of ampicillin anhydrate particles. The new brass bushings were constructed and installed in all four pump manifolds.

3. Indexer Program

Finally, in verifying the indexer program during the preflight ground operations, we detected a deviation in the one of the values controlling the duration of pump motor rotation in three of the fifty pump motor rotation subroutines. Because the deviation was minor, we did not correct the indexer program during the preflight ground operations. However, after verifying that the deviation was incorrect after the launch scrub, we subsequently corrected the indexer program by entering the proper value.

B. Second Preflight Ground Operations

The second preflight ground operation was performed on Cape Canaveral Air Force Station by members of the MIS-B ground operations team which include representatives from the U.S. Air Force integration office, Aerospace Corp., Muniz Engineering, Inc., and SBS. We performed the second preflight ground operation on July 2, 1995, through July 6, 1995, to support the July 13, 1995, launch of STS-70. The MIS-B hardware was successfully preflighted during this operation and received NASA flight certification. The hardware was turned over to NASA for installation in the Orbiter on July 7, 1995. No problems occurred in installing the hardware in the Orbiter and testing the electrical power circuits.

During the second preflight ground operation, we encountered some of the same problems in mix motor stalling as in the first preflight ground operation. Although the brass bushings sealing the mix motor shaft performed well without suspension in the pump, mix motor did stall after the pumps were charged with polymer/drug suspension. We suspect that it was the ampicillin anhydrate particles again which caused the mix motors to stall. The particles of ampicillin anhydrate infiltrated between the bushing and the mix motor shaft causing the shaft to seize. However, we were able to achieve adequate free rotation of the mix motor shafts by running the mix motors for extended periods of time. This action "burned in" the bushings and allowed for free rotation of the mix motor shafts. However, in subsequent leak testing, we found that significant leaks occurred in the mix

motor shaft seals. One was large enough to require that the pump be rebuilt and a new O-ring installed during the prelaunch ground operation.

C. Postflight Ground Operations

Postflight ground operation was performed on Cape Canaveral Air Force Station by members of the MIS-B ground operations team which include representatives from the U.S. Air Force integration office, Aerospace Corp., Muniz Engineering, Inc., and SBS. We performed the second preflight ground operation on July 20, 1995, through July 23, 1995, to support the July 20, 1995, landing of STS-70.

External examination of the MIS-B hardware showed no defect or damage. Upon disassembly of the hardware to the primary containment level, all pumps were observed to be in the fully discharged position. This indicated that all four pumps functioned. We then disassembled the hardening chambers.

1. Disassembly

Upon disassembly of hardening chambers 1 and 3, we discovered that the polymer solution for chamber 1 and polymer/drug suspension for chamber 3 had been successfully sprayed into the chamber. Examination of the internal surfaces of these hardening chambers indicated that a significant portion of the test fluid had impinged on the hardening chamber surface opposite the spray nozzle and had dried to a film. In addition, microspheres were visible on all internal surfaces. Some internal surfaces collected more microspheres than others. These surfaces were the Teflon® backfill tube and the exposed ceramic surfaces of the piezoelectric recirculation fan. The microspheres and films present in these hardening chambers were collected from these surfaces and stored in a sealed container. The yield of microspheres was not as large as anticipated. The microspheres were affected by static electricity.

Upon disassembly of hardening chambers 2 and 4, we discovered that a significant portion of the test fluids in both hardening chambers had dried into a mass at the end of spray nozzle. The polymer masses were also discolored indicating that the polymer had been subjected to heat. This would be expected if the polymer had stuck to the spray nozzle because the tip of the spray nozzle generates heat. Some microspheres were present on the internal surfaces of these hardening chambers but not in the quantities present in hardening chambers 1 and 3. Note: The spray nozzles for hardening chambers 1 and 3 are powered from the same power supply while the spray nozzles for hardening chambers 2 and 4 are powered from another power supply. The microspheres and polymer masses present in these hardening chambers were collected from these surfaces and stored in a sealed container. The yield of microspheres was not as large as anticipated.

2. Safety Relief Valve Operation

During the disassembly of the MIS-B hardware for post-flight cleaning, we discovered that the safety relief valves associated with hardening chambers 2, 3, and 4 had been activated. This was indicated by the presence of polymer or polymer/drug on the outside of the safety relief valve and in the adsorbent container. Activation of the safety relief valve indicates that back-pressure in excess of approximately 65 psig occurred somewhere in the plumbing system during pumping. Due to the presence of polymer or polymer/drug product in the hardening chamber and on the ultrasonic spray nozzle tip, we can conclude that the ultrasonic spray nozzles for hardening chambers 1, 2, and 4 clogged during spraying. This resulted in a reduction in the yield of polymer or polymer/drug microspheres.

A possible explanation for the ultrasonic spray nozzle clog is the excess heat generated by the stirring motors during operation coupled with the low spray rate. Another possible explanation for this observation is that the nozzles and power supply for hardening chambers 2 and 4 were not as closely matched as the nozzles and power supply for hardening chambers 1 and 3. Each power supply and nozzle set is tuned at the factory to produce the highest resonance efficiency. If the tuning is not correct, then the nozzle resonance efficiency drops and the excess energy is converted to heat. If the power supply and nozzles for hardening chambers 2 and 4 were not tuned properly, then these nozzle tips would be hotter than the nozzles in hardening chambers 1 and 3.

In addition, the clogging of the ultrasonic nozzles for experiments 3 and 4 indicate that the polymer/drug suspension is more susceptible to precipitation on the nozzle tips than the solution containing only polymer. This result is not unexpected due to the fact that the presence of particulates in a processing stream can affect flow properties and subsequently spraying dynamics. The concentration of polymer in the polymer/drug suspension for hardening chamber 2 and 4 was 7.50 wt% when referenced to the total suspension weight (including ampicillin anhydrate) but increases to 7.82 wt% when referenced to only ethyl acetate. The concentration of polymer in the polymer solution used in hardening chambers 1 and 3 was increased to 7.82 wt% to be the same as in the polymer/drug suspension when referenced to ethyl acetate. The observation that the polymer/drug suspension precipitated more readily on the tips of ultrasonic spray nozzles for hardening chambers 2 and 4 indicates that the presence of ampicillin anhydrate influenced the spraying dynamics.

Two possible solutions to this problem can be suggested. First, the ultrasonic power supply for spray nozzles 2 and 4 should be retuned for maximum efficiency. Second, the pump rate can be increased rate slightly. Doubling the pump rate may prevent spray nozzle clogs by increasing the amount of polymer/drug suspension presented on the nozzle tip. By increasing the mass flow rate to the nozzle tip, the probability of the polymer or polymer/drug precipitating on the tip will be reduced. The flow rate to the nozzle tip can be optimized to balance both a slow spraying rate to better utilize the hardening chamber volume and a fast spraying rate to prevent ultrasonic nozzle tip precipitation.

3. Piezoelectric Recirculation Fan Operation

In examining the piezoelectric recirculation fan, we found polymer or polymer/drug product adhered to the fan blades. In addition, not many microspheres were found in the fan conduit - an indication of low or nonexistence flow through the conduit. Therefore, we conclude that the piezoelectric recirculation fan did not have its intended effect on the microdroplet spray produced by the ultrasonic spray nozzle on-orbit. This conclusion is also supported by the formation of a polymer or polymer/drug film on the end of the hardening chamber opposite the spray nozzle in hardening chambers 1 and 3. The film formation was reduced in hardening chambers 2 and 4 due to the clogging of the ultrasonic spray nozzles.

However, due to the film formation evident from the operation of MIS-B on-orbit, some sort of mechanism is needed to disrupt the stream-lining of the spray produced by the ultrasonic spray nozzle. This stream-lining of the spray is probably responsible for the formation of the polymer or polymer/drug film by causing the microdroplet stopping distance to be longer than the hardening chamber. Two possible mechanisms can be suggested to disrupt the stream-ling effect: (1.) gimbal the spray nozzle to impart a rotational or side-to-side motion or (2.) incorporate a fan or air baffles close to the nozzle tip to impart an gas-phase current to swirl the spray. The first option is possible but would require extensive modification of the MIS-B hardware. The second option is a low-cost alternative. And, the piezoelectric fan could be relocated to the nozzle end of the hardening chamber to direct a gas-phase flow onto the nozzle tip without much hardware modification.

4. Dust Problem with Silica Gel

In microscopically examining the silica gel contained in the absorbent containers, we found that silica gel dust was present. Some of these silica gel dust particles were of the same size as the space-made microspheres. Therefore, a possibility exist that the microspheres made by MIS-B were contaminated by silica gel dust. Surface analysis of the space-made product indicated presence of silicon. The silicon contamination may also be responsible for the discoloration observed in the space-made product.

This dust problem can be alleviated by removing the dust inherently associated with the silica gel beads before loading the beads into the MIS-B hardware. The dust can be removed by washing the beads in a suitable solvent, collecting the beads by filtration, and drying. Alternatively, the beads could be cleaned by vacuuming or by fluidization in an air stream.

5. Discoloration of Product

We observed a green discoloration in the some of polymer or polymer/drug microspheres and films samples produced by MIS-B. In an attempt to determine the source of this discoloration, we paid particular attention to the polymer or polymer/drug residues found in the plumbing systems of MIS-B during disassembly and cleaning. To this end, we did not find any discolored residue in the syringe pump barrel, but found discolored residue deposited in the absorbent containers by the

activation of the safety relief valve. This leads to the hypothesis that the discoloration is caused by the interaction of the polymer or polymer/drug with silica gel.

Evidence to support this hypothesis is found in research performed by personnel of Birmingham Polymers, Inc. - the supplier of the polymer. In research unrelated to the MIS-B project, a green discoloration of a polymer similar the poly(DL-lactide-co-glycolide) used in MIS-B was observed. It was hypothesized that the green discoloration was caused by chelating reactions occurring between free metals and the polymer because many chelating reactions can result in color manifestations. In addition, amorphous silica from which silica gel is produced can form chelate-type bonds with some oxygen- and nitrogen-containing organic compounds. The polymer used in the MIS-B experiments is an oxygen-containing organic compound. Therefore, we can hypothesize that the polymer formed chelate-type bonds with the silica gel resulting in the green discoloration.

This problem can be alleviated by removing the dust inherently associated with the silica gel beads before loading the beads into the MIS-B hardware. Methods to clean the silica gel beads were discussed in section above. An alternative solution would be to change the absorbent type.

6. Solenoid Valve Operation

During the cleaning of the MIS-B hardware, we could not remove the solenoid valves for hardening 1, 2, and 4 from their respective pump manifolds. In the current hardware design, the valve is recessed too far into the pump manifold. This prevents a tool from contacting a hard point on the valve body. The only accessible part of the valve is a protective sleeve which rotates around the valve body when trying to remove the valve. Therefore, the pump manifold needs to be modified to allow for access to a hard point on valve body. This can be easily accomplished by slightly enlarging the cavity on the pump manifold into which the valve is placed.

D. Characterization of Microspheres

Upon examination of the space-made and earth-made microspheres, the following observations were made.

1. Earth-made microspheres were a fine white powder, while space-made microspheres were black to green in color. The space-made microspheres had very little resemblance to powder.

2. Earth-made microspheres were a free-flowing powder while space-made microspheres were not. The space-made microsphere sample had large clumps mixed in with the bulk material that would not break-up with a metal spatula.

After initial examinations of the space-made and earth-made microspheres were made, the vials containing the microspheres were placed in a metal paint can containing desiccant (Drierite, W.A.

Hamond Drierite Company: Xenia, Ohio). The paint can was placed in a laboratory freezer (-20°C). The samples of microspheres were stored in this manner until further analysis.

E. Light Microscopy

A small sample of the space-made microspheres was placed on a glass slide and examined using a light microscope (Olympus ULWCP 0.3). We compared the space-made microspheres to earth-made microspheres of the same composition. Comparing earth-made placebo microspheres to space-made placebo microspheres, we observed earth-made placebo microspheres were more symmetrical in shape and had smoother surfaces than space-made placebo microspheres. Comparing earth-made ampicillin microspheres to space-made ampicillin microspheres, we observed earth-made ampicillin microspheres were symmetrical in shape but had wrinkled edges. Space-made ampicillin microspheres were somewhat symmetrical in shape, but the sample contained a lot of material which had little resemblance to spherical particles. The particles that were spherical did not appear to have wrinkled edges. Both lots of ampicillin microspheres when observed with the microscope were very dark in color compared to placebo microspheres.

F. Scanning Electron Microscopy

To examine the space-made microspheres by scanning electron microscopy (SEM), we mounted a small sample of the space-made microspheres on a specimen stub and sputter-coated (Technics Corporation, Hummer V) the microspheres with 60:40 gold/palladium. We also used silver to coat the microspheres. We then examined the coated microspheres (ETEC Corporation, Autoscan). A sample of the earth-made microspheres was prepared in a similar manner.

We made following comparisons:

Earth-made placebo microspheres were spherical particles and for the most part had smooth unblemished surfaces. Cross-sections of earth-made placebo microspheres show a solid inner- core throughout. Figure 1 (a, b, c) shows micrographs taken of earth-made placebo microsphere samples.

Space-made placebo microspheres were a mixture of spheres and various other non-spherical particles (ie. flakes, many fused spheres). Space-made placebo microspheres had smooth surfaces and cross-sections show a solid core. Figure 2 (a, b) shows micrographs of space-made placebo microsphere samples.

Earth-made ampicillin microspheres were spherical in shape with many indentions and crevices. The surfaces of earth-made ampicillin microspheres were very wrinkled and cross-sections revealed a porous core. Figure 3 (a, b, c) shows micrographs of earth-made ampicillin microsphere samples.

Space-made ampicillin microspheres were a mixture of spheres and various other non-spherical objects (ie. flakes, many fused spheres). Space-made ampicillin microspheres had smoother

surfaces than earth-made ampicillin microspheres and cross-sections revealed a less porous core than earth-made ampicillin microspheres. Figure 4 (a, b) shows micrographs of earth-made ampicillin microsphere samples.

G. Atomic Spectroscopy

In order to determine the drastic differences in earth-made verses space-made microspheres, we also examined the atomic spectrum of the microspheres (Kevex, microanalyst 7500). Sample preparation was the same as for scanning electron microscopy. Table 1, lists the elements that were present.

Table 1: Atomic Spectrum Analysis of Earth-made and Space-made Microspheres

Sample ID No.	Location	Description	Elements
H597-062-02	space-made	placebo microspheres	carbon, oxygen, silicon
H597-062-04	space-made	ampicillin microspheres	carbon, oxygen, silicon, sulfur
H597-065-01	earth-made	placebo microspheres	carbon, oxygen
H597-065-02	earth-made	ampicillin microspheres	carbon, oxygen, sulfur

Figures 5, 6, 7, and 8 are low magnitude atomic scans of microsphere samples. The presences of gold(AU), palladium (PD), silver (Ag), chlorine (Cl), Iron (Fe) and copper (CU) are due to the coating material used to coat the microspheres. In order to determine sulfur, we used a silver coating because of the interference of sulfur and gold.

The presence of sulfur in earth-made microsphere Lot H597-065-02 (Figure 6 a, b ,c) and space-made microsphere Lot H597-062-04 (Figure 7 a, b, c) can be explained because ampicillin has sulfur in it. We examined low magnitude scans along with higher magnitude surface scans and cross-section scans for sulfur. The actual ampicillin content of these two microspheres lots has not been determined.

We examined space-made microspheres from the first space microencapsulation experiment for sulfur and silicon. Atomic spectroscopy results (Figure 8 a, b, c) showed the existence of both. We expect the silicon came from small dust particles of silica gel floating in the hardening chambers. The earth-made microspheres would not be contaminated to silica gel dust particles on earth because they would not float during the drying period. Future experiments could be attempted using another drying material instead of silica gel or the silica gel dust particles should be removed. It is also possible of a chemical chelate reaction occurring between silicon and the excipient polymer (poly DL-lactide-co-glycolide, Birmingham Polymers, Birmingham, Alabama). This proposed reaction could cause the drastic differences between space-made microspheres and earth-made microspheres. We

examined the first microencapsulation experiment space-made microspheres for such differences. The microspheres were a fine powder but were somewhat gray in color.

H. Differential Scanning Calorimetry

Figure 9 (a, b, c) shows the results of differential scanning calorimetry (DSC) performed on both space-made and earth-made microspheres. The scans for the samples were extended out to the decomposition temperature of the excipient polymer, poly(DL-lactide-co-glycolide), (Birmingham Polymers, Birmingham. Alabama).

The exothermic peaks above 200°C in both DSC scans of space-made ampicillin microspheres (Figure 9 D) and earth-made ampicillin microspheres (Figure 9D) could be due to the decomposition of ampicillin. DSC scans of placebo microspheres do not show such peaks while a DSC scan of ampicillin, Figure 10, shows the above 200°C profile. The literature states that ampicillin decomposes around 199- 202 °C.

Using conventional glass transition analysis, the microsphere samples had the following average transition temperatures:

Table 2: Glass Transition Temperatures of Earth-made and Space-made Microspheres

Sample ID No.	Location	Description	Glass Transition Temperature, °C
H597-062-02	space-made	placebo microspheres	39.0
H597-062-04	space-made	ampicillin microspheres	39.5
H597-065-01	earth-made	placebo microspheres	38.0
H597-065-02	earth-made	ampicillin microspheres	36.5

Also with regards to the glass transition range and temperature, we compared microsphere samples verses the excipient DL-PLG. Figure 11 and Figure 12 are DSC scans of earth-made microspheres and space made microspheres verses the excipient. These DSC scans show the reduction of glass transition temperature from 50°C for the excipient to an average of 38°C for microsphere samples. The reduction of temperature could be the result of residual solvent from the microsphere encapsulation process. The excipient solvent ethyl acetate was held common to the microsphere production of earth-made and space-made microspheres. Also when compared against the excipient, the glass transition ranges for microsphere samples are not very defined. Because the glass transition ranges for microsphere samples were not very defined, we were not able to accurately measure their enthalpy of fusion.

VII. CONCLUSIONS

Based on the results obtained from the postflight disassembly of the MIS-B hardware, several conclusions can be reached and recommendations for modifying the hardware to increase the operational success of MIS-B in future flights can be made. These recommendations are as follows for the problems identified in the results section:

Mix Motor Stalls:

- Limit the mixing time to a shorter amount, possibly 5 minutes. Currently, the mix motors function throughout the spraying time of 2 hr. By reducing the mixing duration, the total heat generated by the mix motors while they operate would be reduced.

- Use only solutions as the test fluid in future missions and not suspensions. Using solutions would prevent the mix motor shaft seal problems currently encountered with MIS-B.

- Change the O-ring configuration for the mix motor shaft. Currently, the seal design for the mix motor shaft, from internal to the pump to external, starts with the internal bushing, an O-ring, and an external bushing. To prevent particles from jamming between the mix motor shaft and the internal bushing, the O-ring can be located inside the internal bushing. As a result, the mix motor shaft seal design would be O-ring, internal bushing, and external bushing. To accomplish this design change, new bushings could be constructed in which the internal bushing had an O-ring groove.

Polymer Precipitation on the Nozzle Tips:

- Retune the ultrasonic power supply for spray nozzles 2 and 4 for maximum efficiency. This would reduce the heat generated by these ultrasonic spray nozzles. Each power supply and nozzle set is tuned at the factory to produce the highest resonance efficiency. If the tuning is not correct, then the nozzle resonance efficiency drops and the excess energy is converted to heat. If the power supply and nozzles for hardening chambers 2 and 4 were not tuned properly, then these nozzle tips would be hotter than the nozzles in hardening chambers 1 and 3.

- Increase the pump rate slightly. An increased pump rate would have two primary effects: inhibit the precipitation of polymer on the spray nozzle tips during operation and shorten the operational time.

Spray Stream-lining:

- Relocate the piezoelectric fan to the nozzle end of the hardening chamber to direct the gas-phase flow onto the nozzle tip to disrupt stream-lining of the spray. Apparently, the stopping distance for a spray of droplets is greater than the stopping distance for a single droplet in microgravity. This would be especially true in the type of low velocity spray produced from ultrasonic spray nozzles as opposed to conventional pressure sprayer nozzles. This is because the spray produced from the ultrasonic spray nozzle is much less turbulent and of a lower velocity than the spray from a conventional pressure spray nozzle. However, because the spray is less turbulent, the spray droplets are able to easily streamline in microgravity and present less air resistance as a whole than as individual droplets. This problem can be corrected by relocating the piezoelectric recirculation fans from the bottom of the hardening chambers where they are currently located to near the spray nozzle tips. In addition, an air shroud can be constructed to fit over the spray nozzle tip containing baffles which would gently swirl the recirculating air around the spray nozzle tip.

Absorbent Problems:

- Remove the dust inherently associated with the silica gel beads before loading the beads into the MIS-B hardware. Or, investigate using a different absorbent that does not possess a dust problem.

Solenoid Valve Access:

- Modify the pump manifold needs to allow for access to a hard point on the solenoid valve body.

Modification of MIS-B Internal Surfaces:

- Based on the observation that some internal surfaces of the hardening chamber attracted more the microspheres than other surfaces, several experiments could be easily designed before the next flight to investigate this phenomenon. The experiments would consist of installing rods of different materials inside the hardening chambers. And, where appropriate, electrically ground some of these rods. The materials used to construct the rods could be chosen for a list of materials (Teflon and ceramic) already incorporated inside the hardening chambers which seemed to attract microspheres and other materials (uncoated aluminum - grounded and ungrounded, uncoated stainless steel - grounded and ungrounded, and other polymers - polyimide, polyaniline, etc.) which may prove better microspheres collectors. In addition, to neutralize the static electricity present in the hardening chambers, ion sources could be installed in the hardening chambers.

In conclusion, the MIS-B experiment was designed and constructed within budget and time schedules. The MIS-B hardware was introduced into the NASA safety review process and subsequently received NASA flight certification for installation aboard the space shuttle. The experiment functioned as expected while on-orbit and was successfully retrieved from the space shuttle. And, although the yields of space-produced microspheres were disappointingly small, enough microspheres were produced for analysis. The recommendations presented above are the result of analyzing the operation of the MIS-B experiment and by examining these observations with those obtained from MIS-A for similarities. By implementing these recommendations, yields of space-made microspheres should be increased if the MIS-B hardware is flown again.

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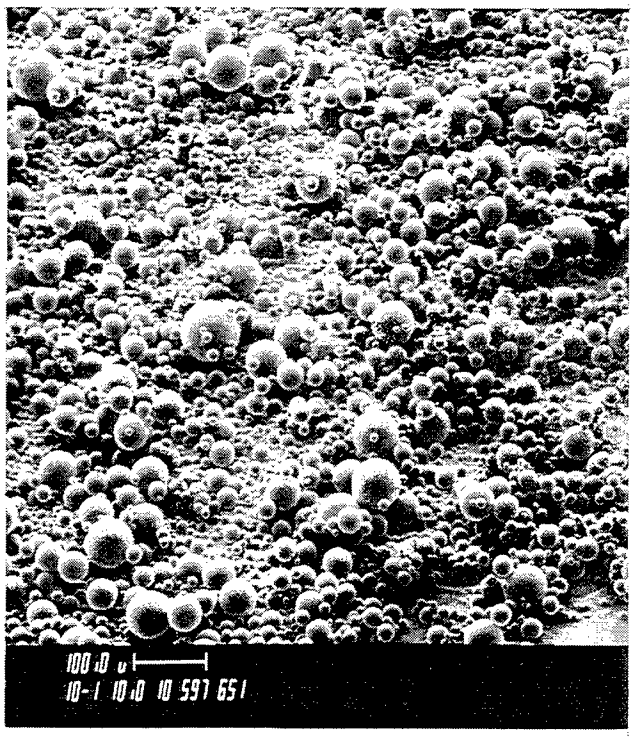
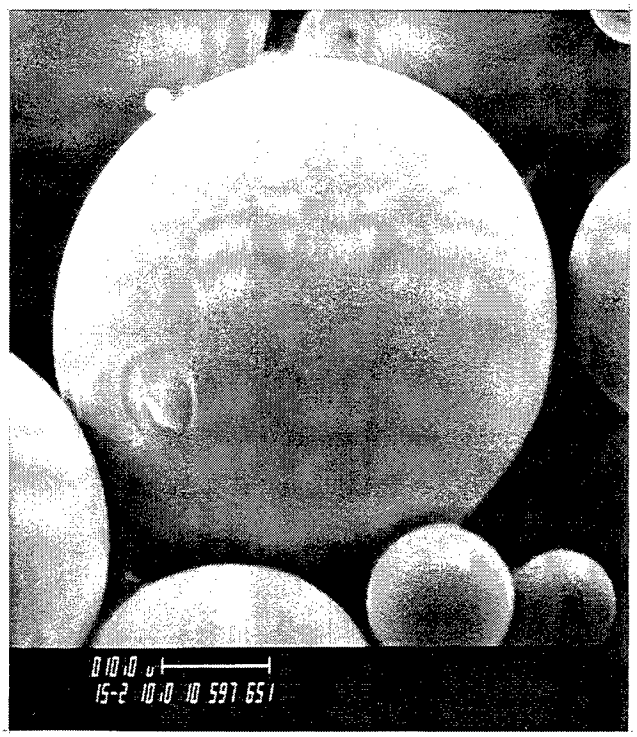
APPENDIX



A



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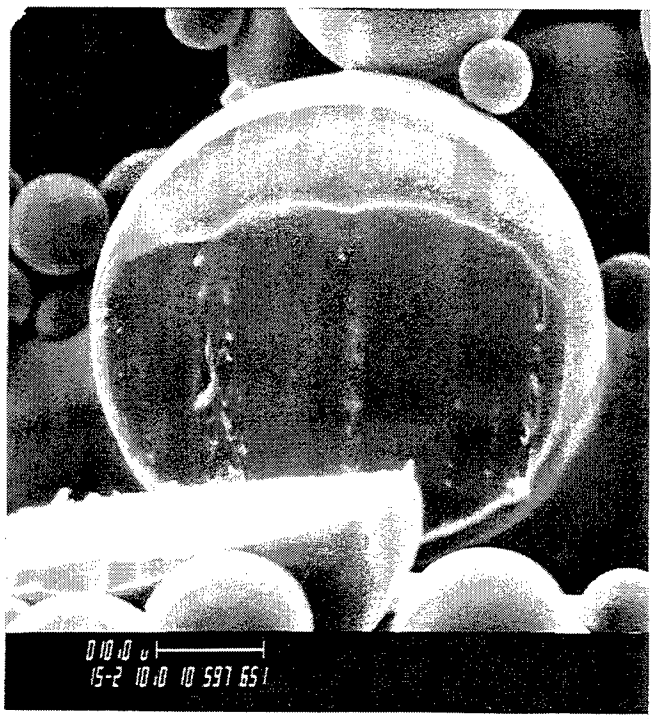
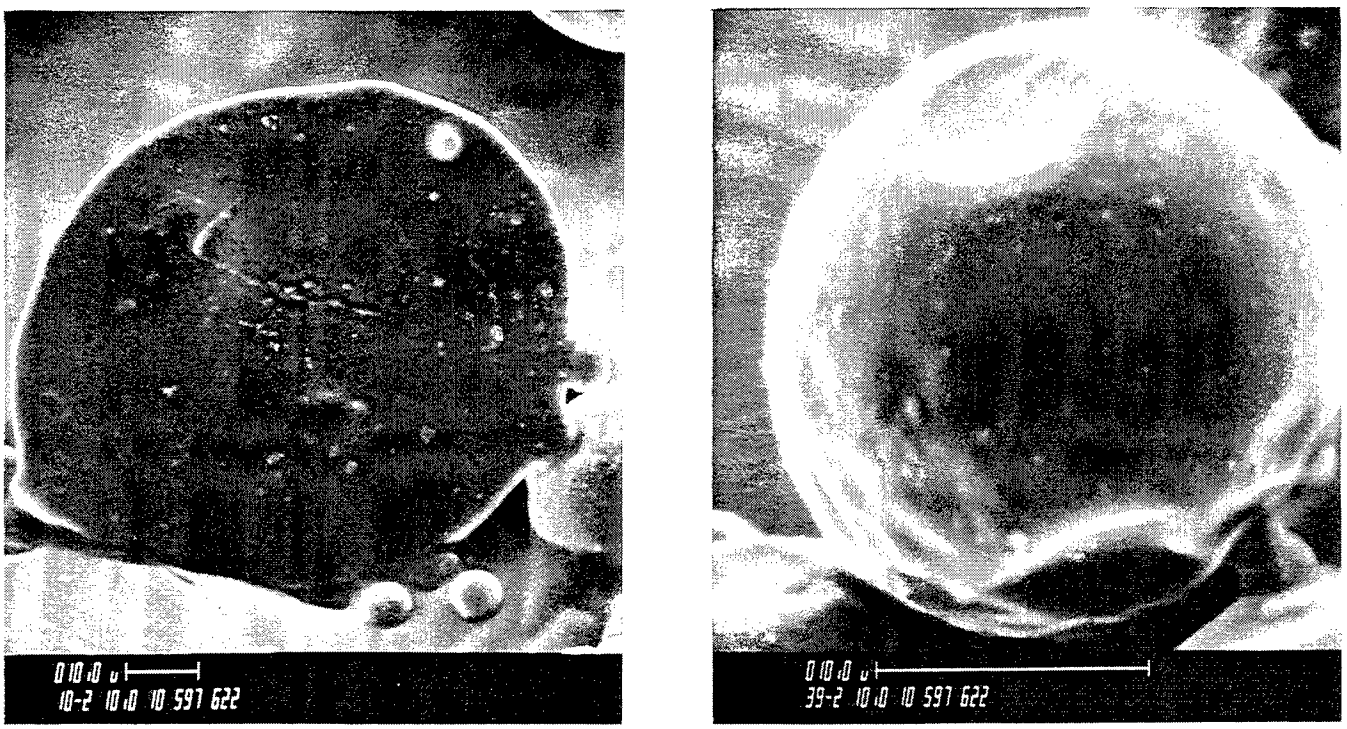


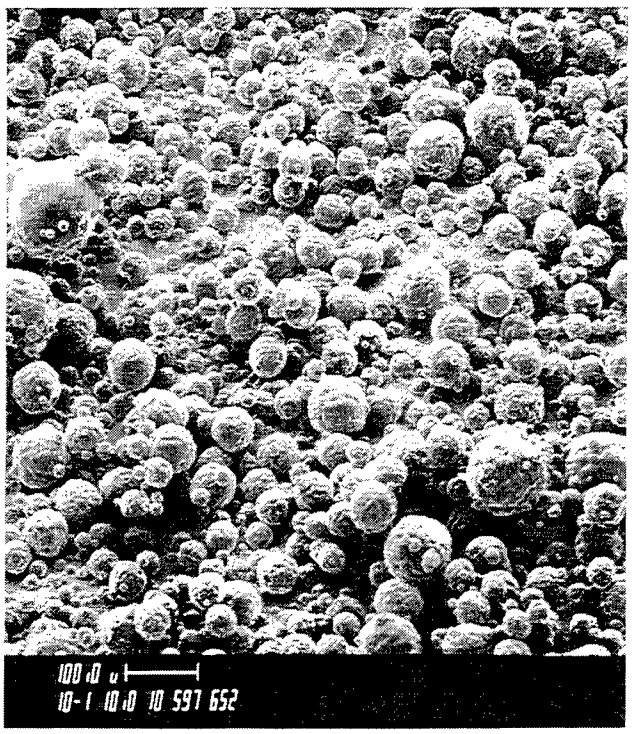
C

Figure 1. Scanning electron micrographs of earth-made placebo microspheres, microspheres lot (H597-065-01).



A B

Figure 2. Scanning electron micrographs of space-made placebo microspheres, microsphere lot (H597-062-02).



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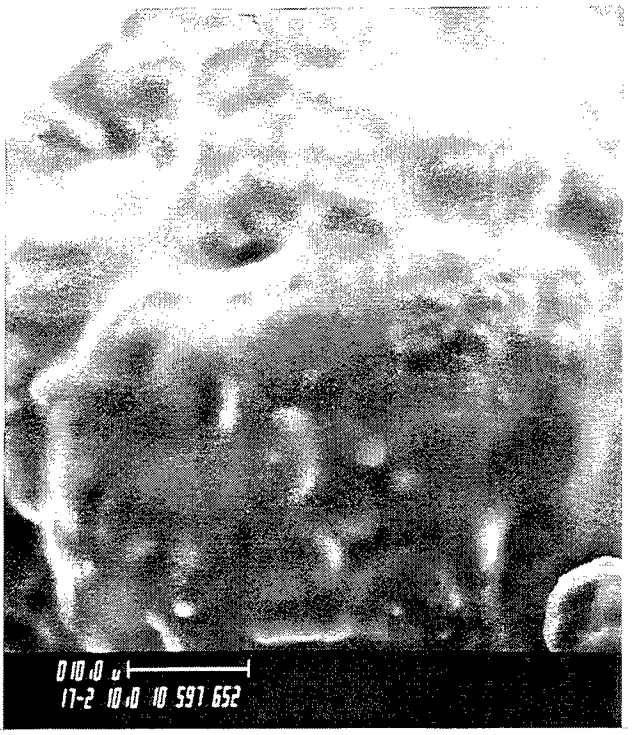

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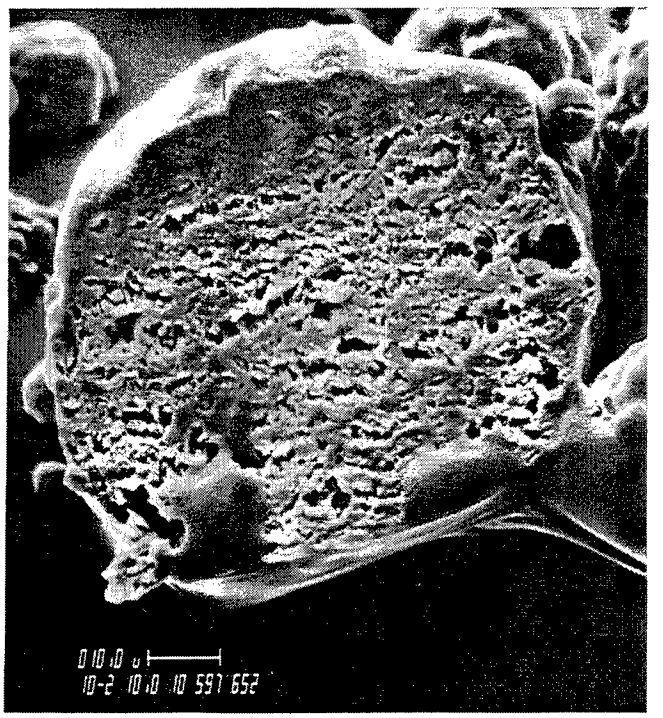
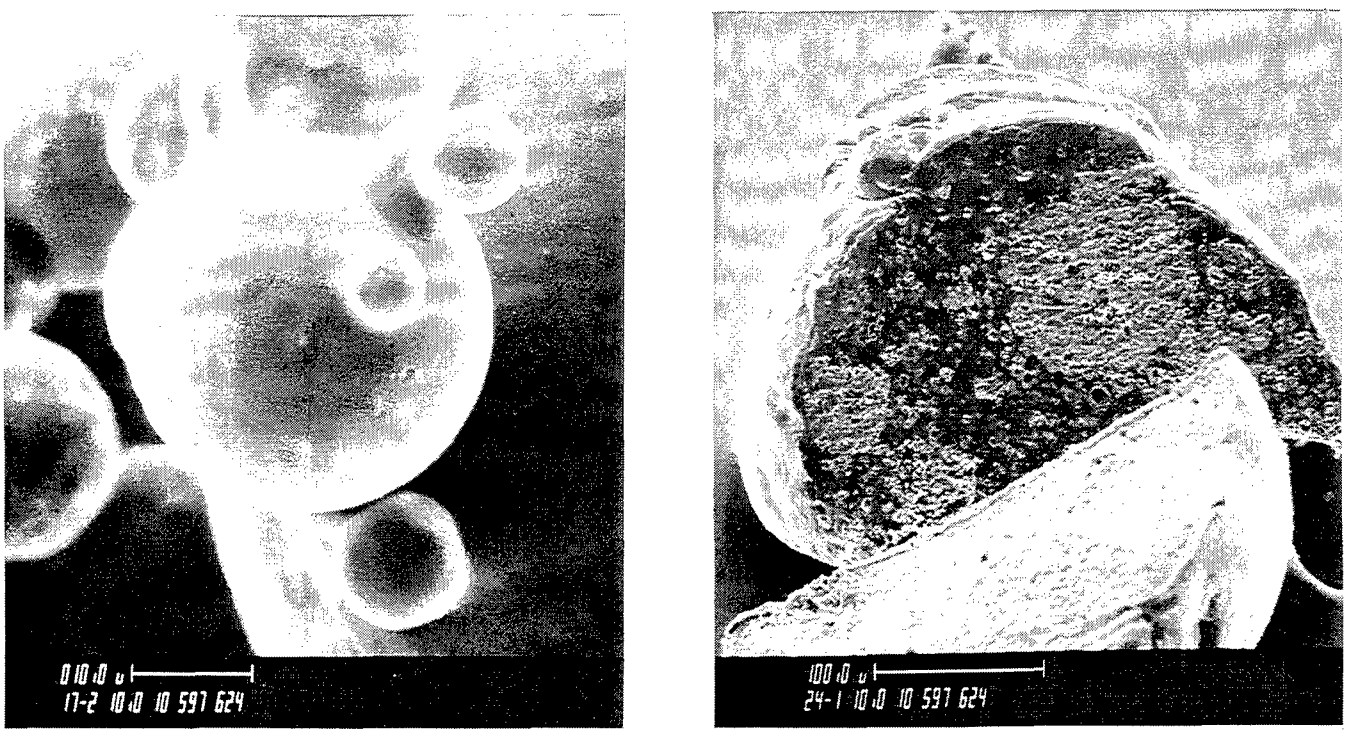


C

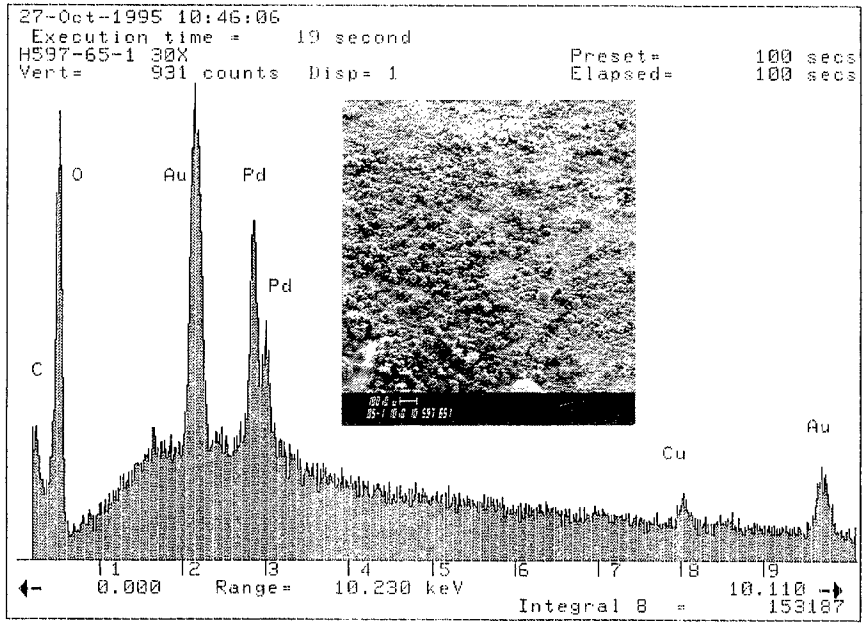
Figure 3. Scanning electron micrographs of earth-made ampicillin microspheres, microsphere lot (H597-065-02).



A B

Figure 4. Scanning electron micrographs of space-made ampicillin microspheres, microsphere lot (H597-062-04).

A



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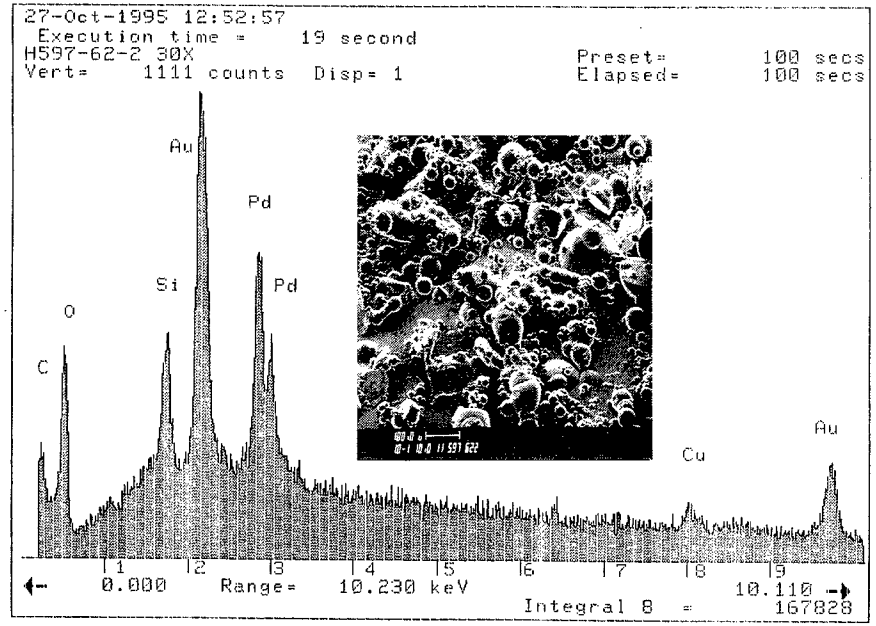
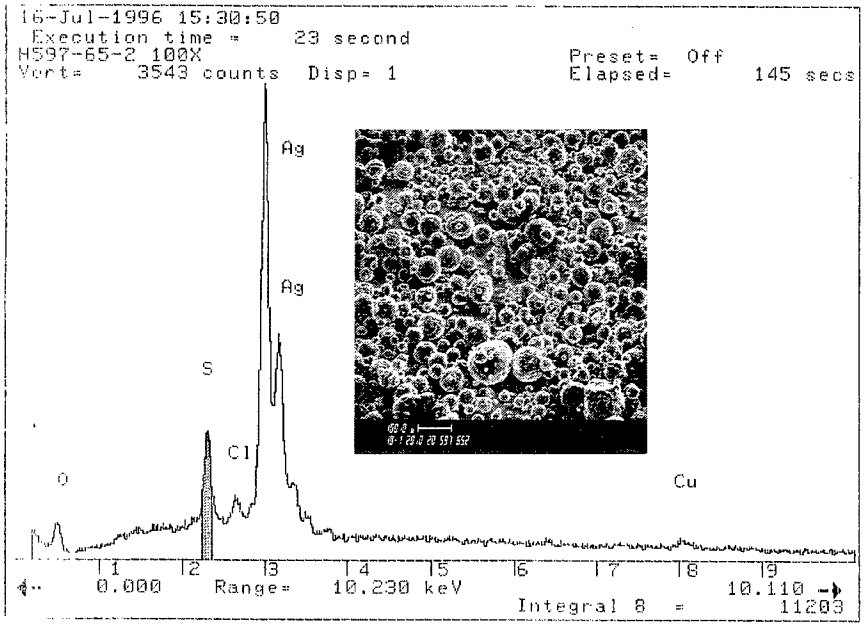
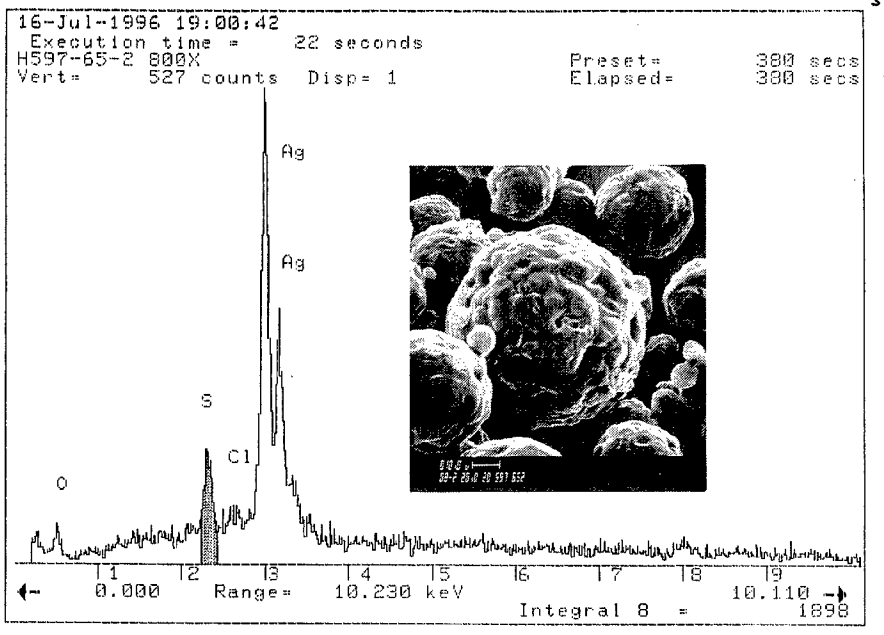


Figure 5: Atomic spectroscopy scans of earth-made placebo microspheres (lot H597-065-1) and space-made placebo (lot H597-062-02) microspheres. Figure A is a scan of earth-made placebo microspheres and Figure B is a scan of space-made placebo microspheres.

A



B



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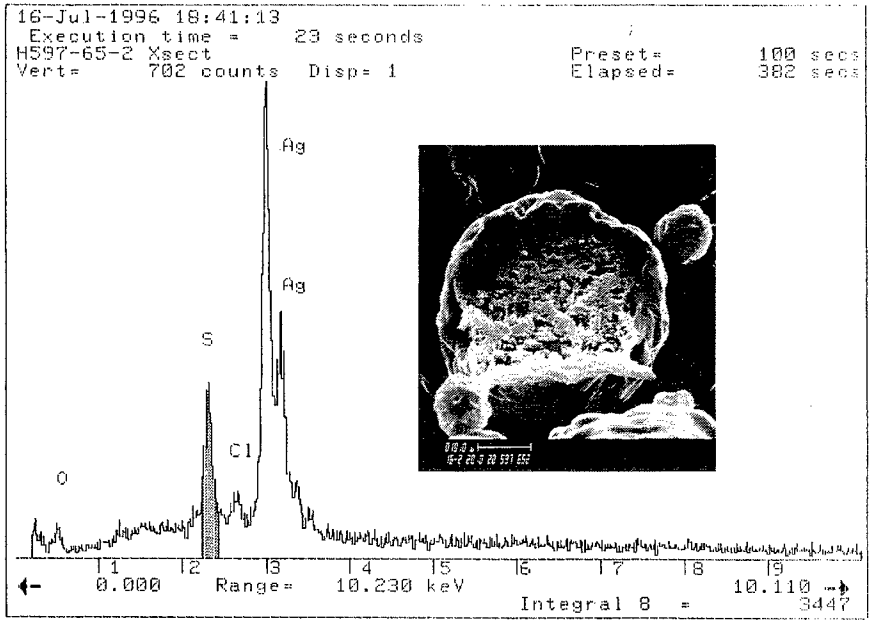
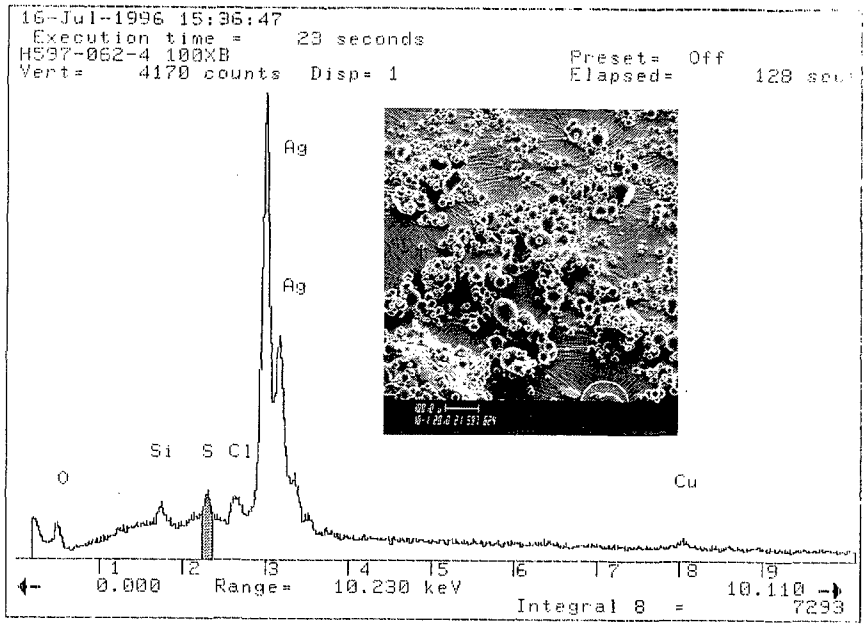
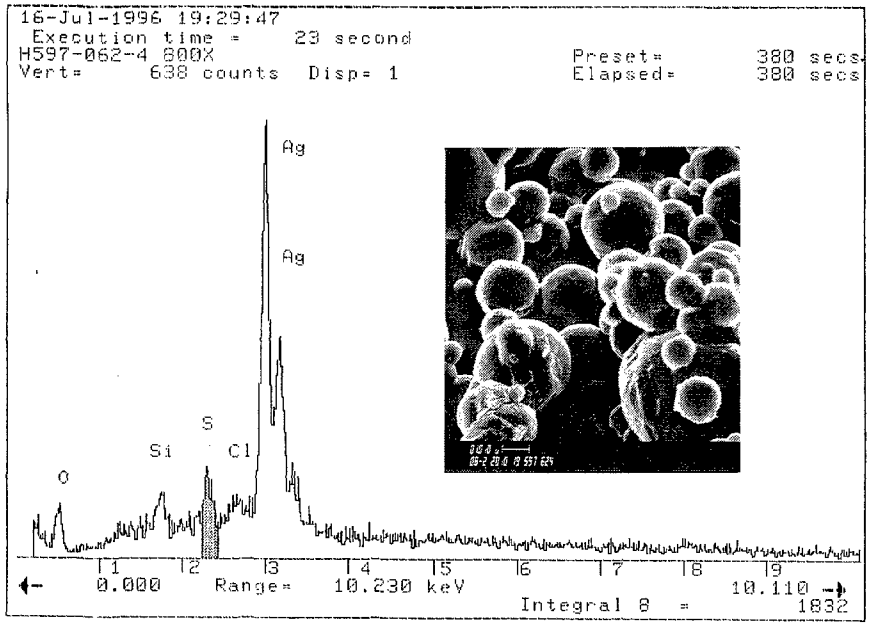


Figure 6: Atomic spectroscopy scans of earth-made ampicillin microspheres (lot H597-065-2). Figure A and Figure B are surface scans while Figure C is a cross-section scan.

A



B



C

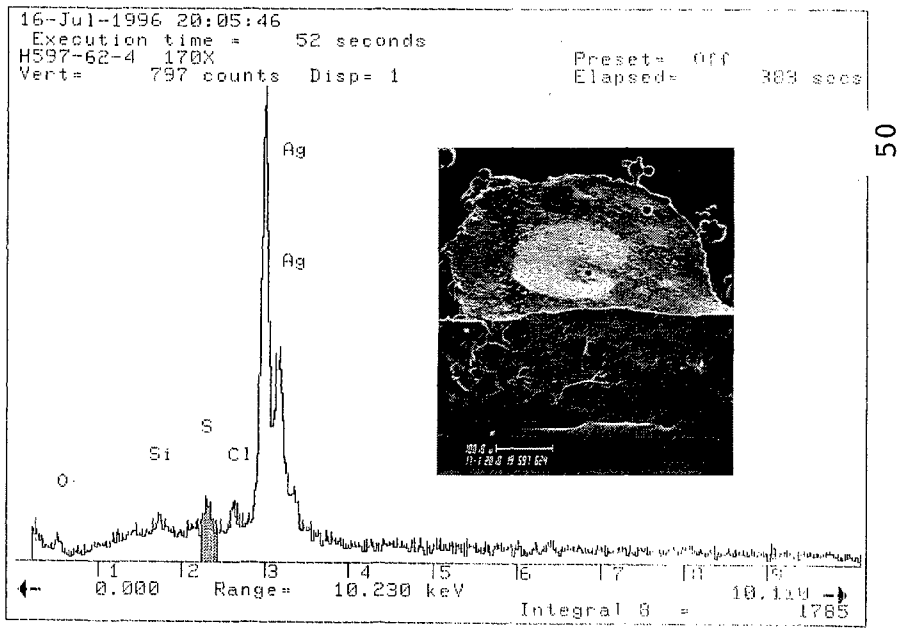
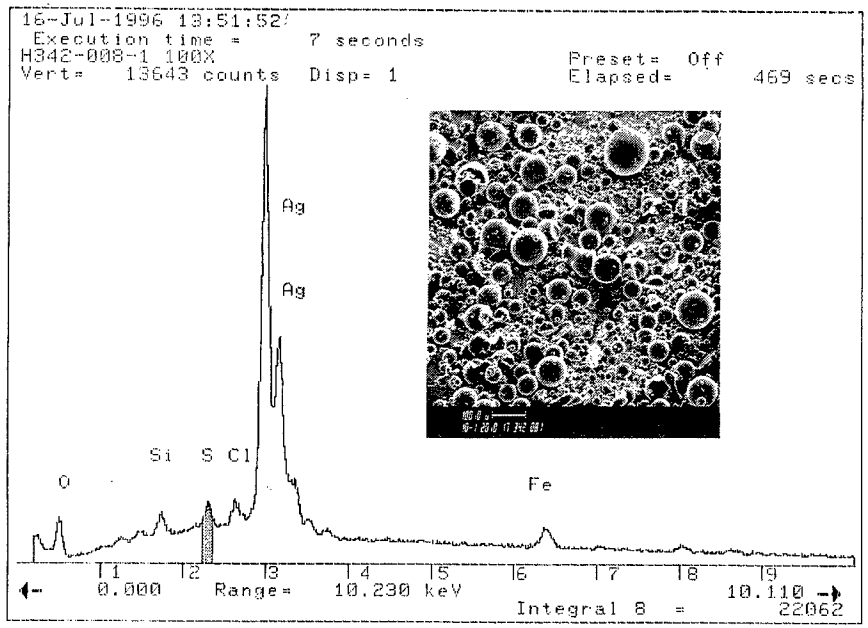
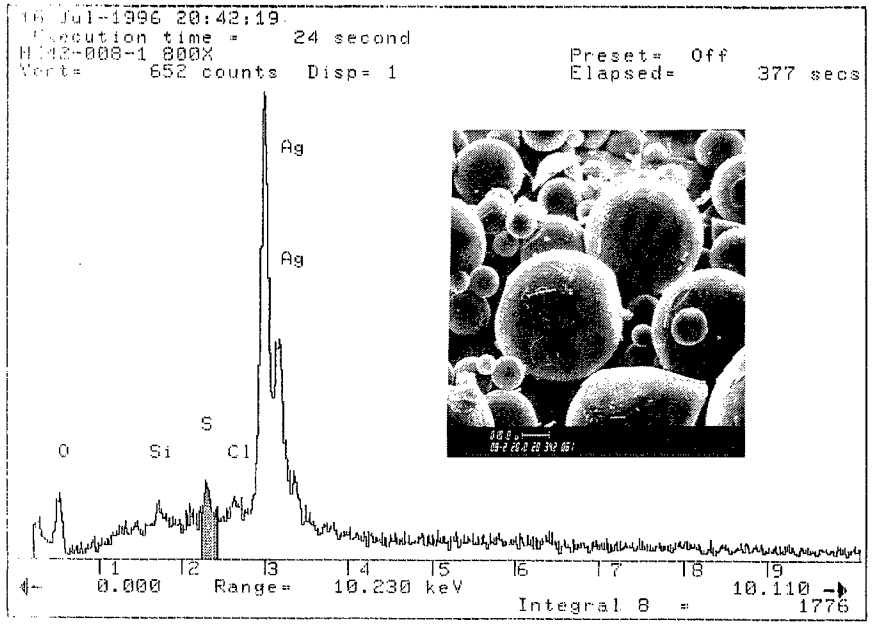


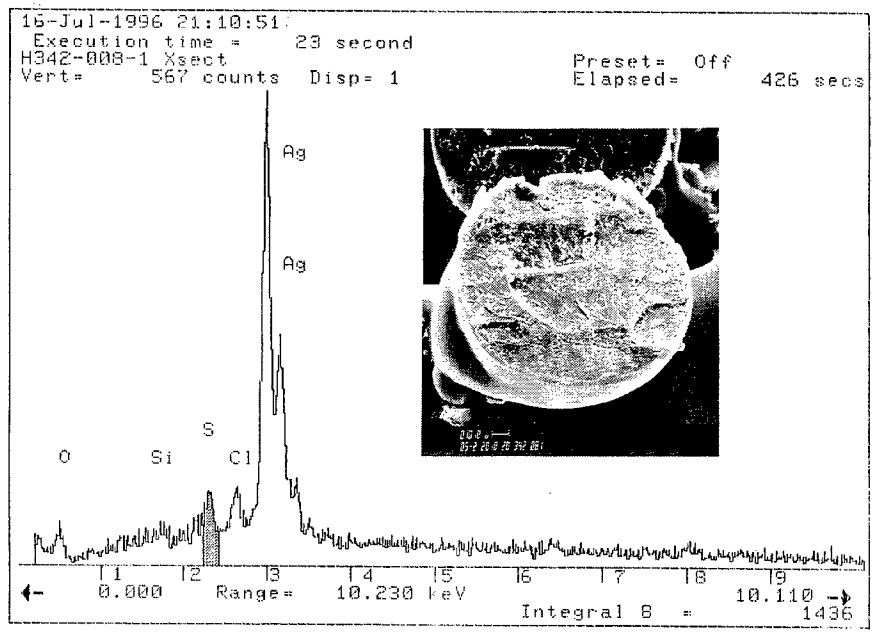
Figure 7: Atomic spectroscopy scans of space-made ampicillin microspheres (lot H597-062-04). Figure A and Figure B are surface scans while Figure C is a cross-section scan.



A



B



C

Figure 8: Atomic spectroscopy scans of space-made ampicillin microspheres (lot H597-008-1). Microspheres prepared during first microencapsulation project(6839). Figure A and Figure B are surface scans while Figure C is a cross-section scan.

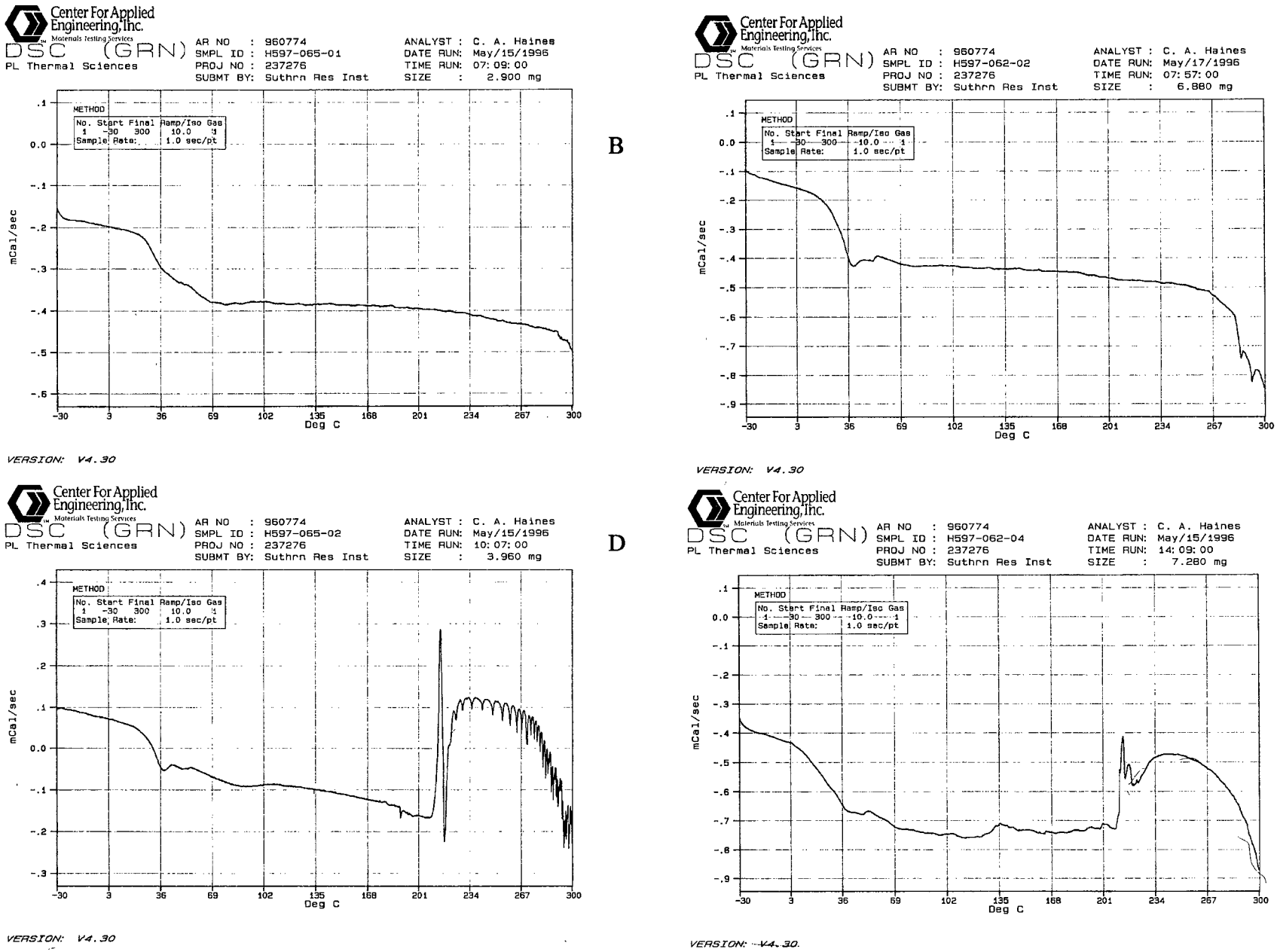


Figure 9: Differential scanning calorimetry thermograms of earth-made and space-made microspheres. Figure A and B are thermograms of earth-made placebo microspheres (lot H597-065-01) and space-made placebo microspheres (lot H597-062-02). Figure C and D are thermograms of earth-made ampicillin microspheres (lot H597-065-02) and space-made ampicillin microspheres (lot H597-062-04).

Center For Applied Engineering, Inc.
Materials Testing Services

DSC (GRN)
PL Thermal Sciences

AR NO : 961121
SMPL ID : Ampicillin Ahy*
PROJ NO : 237305
SUBMT BY: Suthrn Res Inst

ANALYST : S. R. Prince
DATE RUN: Aug/01/1996
TIME RUN: 08:09:00
SIZE : 6.060 mg

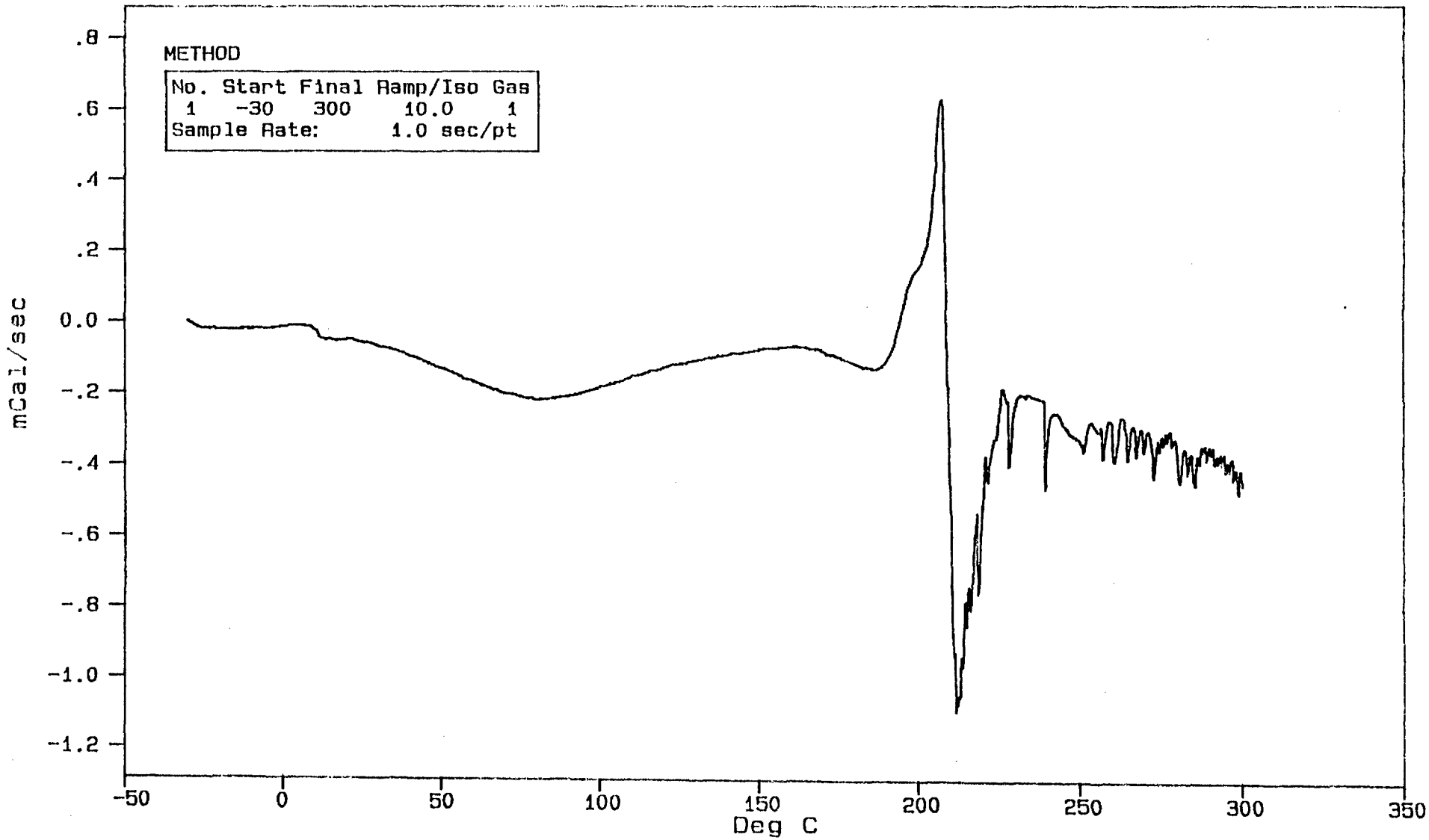


Figure 10: Scanning Differential Calorimetry thermogram of Ampicillin.

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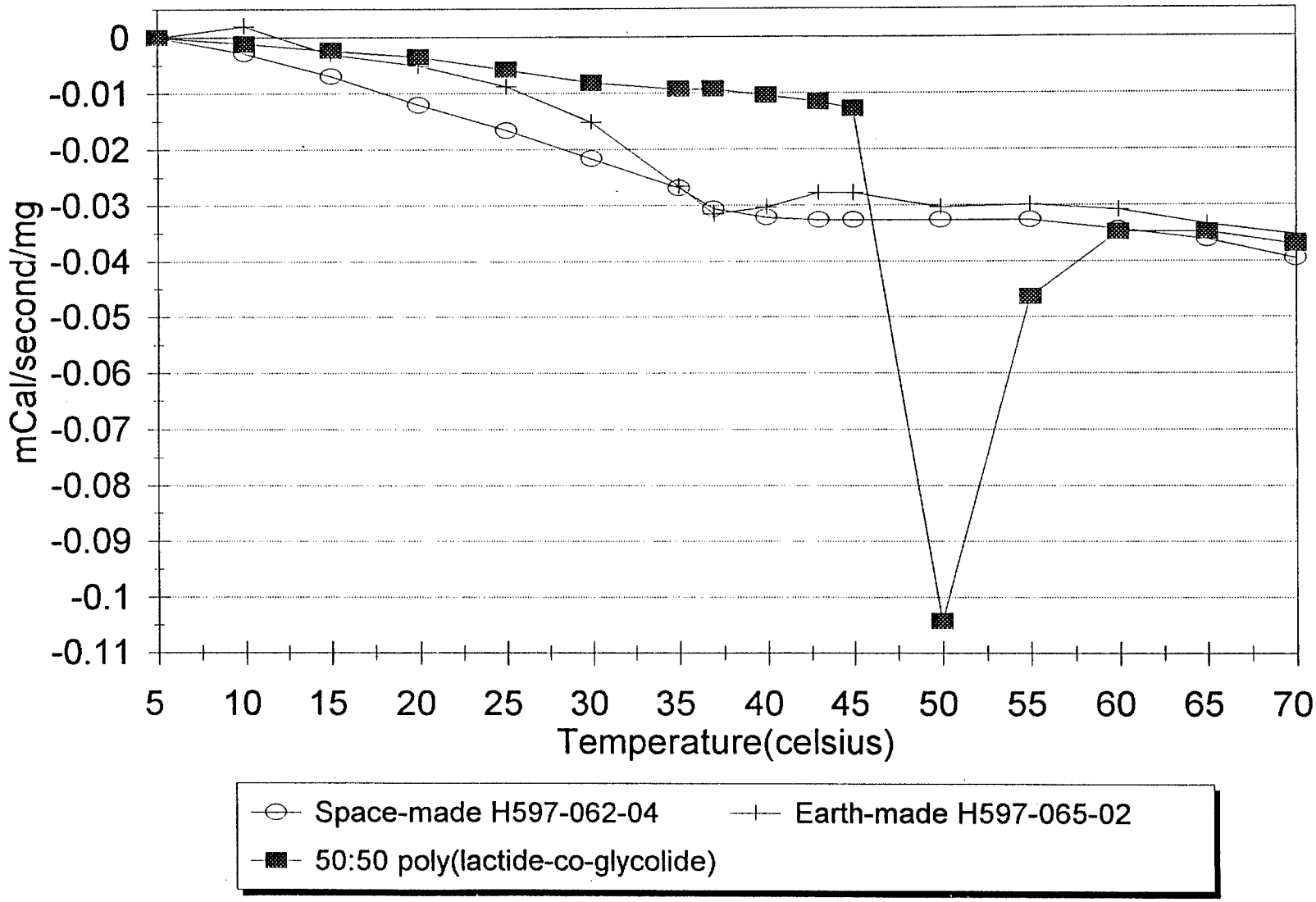

Figure 11: Scanning differential calorimetry thermograms of earth-made and space-made ampicillin microspheres and excipient.

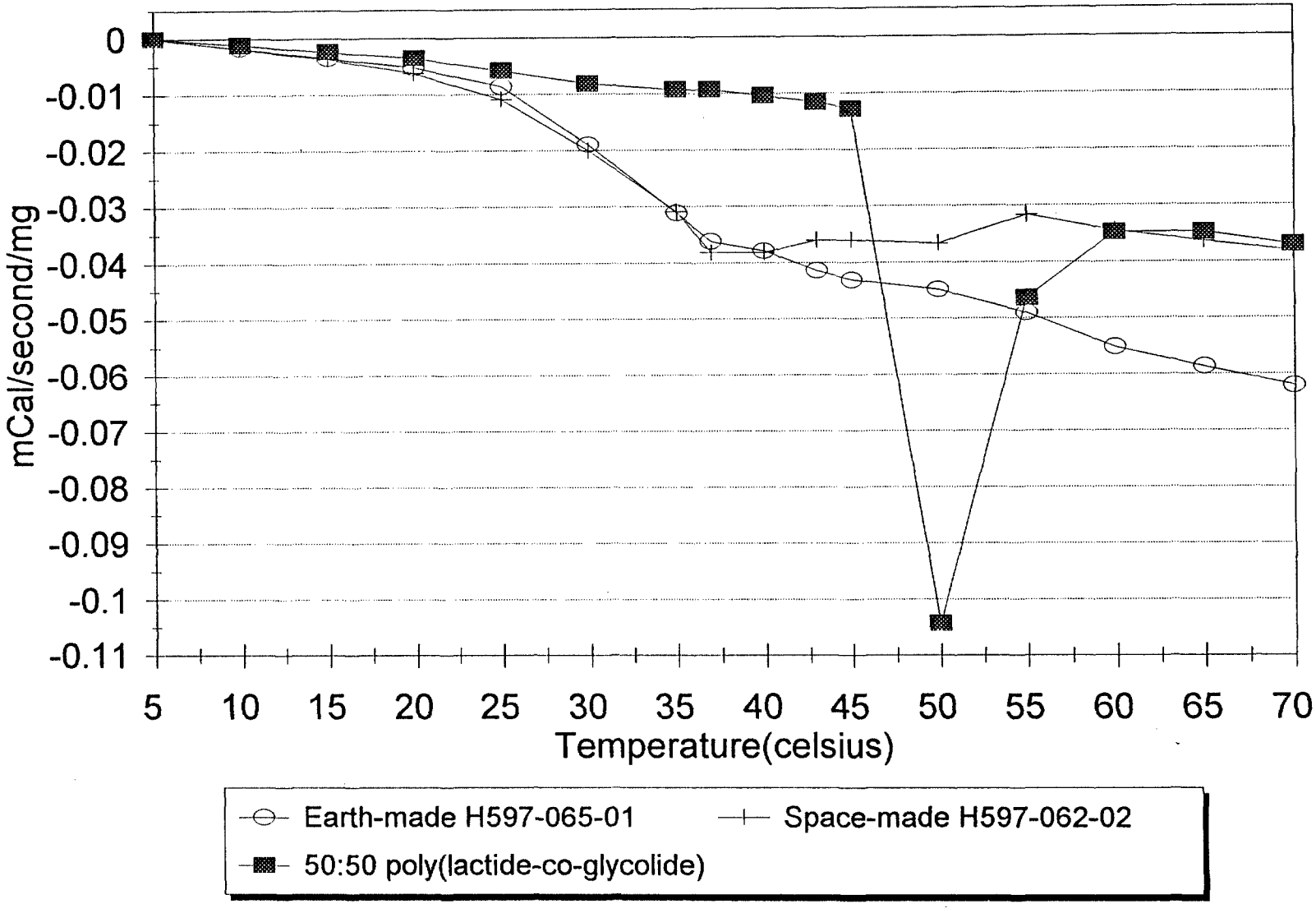

Figure 12: Scanning differential calorimetry thermograms of earth-made and space-made placebo microspheres and excipient.

DEPARTMENT OF THE ARMY
US ARMY MEDICAL RESEARCH AND MATERIEL COMMAND
504 SCOTT STREET
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REPLY TO
ATTENTION OF:

MCMR-RMI-S (70-1y) 2 Feb 98

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FOR THE COMMANDER:

PHYLIS M. RINEHART
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